ENDEAVOUR

A quarterly review designed to record the progress of the sciences in the service of mankind

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The scientist's responsibility

In our present issue, letters from distinguished correspondents raise the question of the place of science in society. The question is one of the first importance, for science profoundly and intimately affects every detail of civilization. Its future influence will inevitably be still greater. But in any discussion of the interrelation of science and society, it is essential to have a precise idea of the relevant connotation of the term 'science.' Among the general public 'science' is frequently used in a sense at once too wide in certain respects, and too narrow in others. Sharper definition attaches to the term if we equate it to 'the sciences,' and it is with this meaning that we employ it here.

The fundamental problem confronting science in the ethical sphere is that of making itself known to mankind as a whole. What fraction of the population of any civilized country—even our own—can be credited with a proper conception of science, its aims, its methods, its results? On the most generous estimate it must be very small. Ignorance of science is by no means confined to the humbler ranks of society. It pervades every walk of life, from the lowest to the highest. It is particularly reflected in the popular press. Each day the newspapers contain elementary errors, misleading references, or out-of-date statements concerning scientific progress and discovery. It is not all their fault. There is nowhere among men of science a general disposition—or indeed ability—to see that the current thought and practice of laboratory and lecture hall are made available to the public through the press, the cinematograph, and other media. There is frequently, it must be confessed, a tendency to avoid contact with the newspaper reporter instead of teaching him to be an accurate and intelligent translator. It is therefore not surprising that the scientific attitude of mind is misunderstood, and even mistrusted, by the public. How slender is the footing which science has won in the popular mind can be inferred from the smouldering fires of astrological superstition, now being fanned into flame by the winds of war. How little even the educated Englishman knows of the achievements of British scientists, either past or contemporary, is shown in his proneness to assume that chemical genius and organization are German monopolies.

The remedy lies in the hands of scientists themselves; and in no country have they a more insistent duty than in Great Britain, for there is no other country with heavier political responsibility overseas, and none whose national characteristic is more typically reticence and understatement. Science, indeed, must become articulate. Even though publicity may be repellent to scientists, they must, as a body, vie with the politicians, for science holds the keys of the future.

There is here an opportunity for concerted action on the part of the various scientific bodies and associations in the British Isles, and indeed in the British Commonwealth of Nations. Certain steps could be taken immediately. The Government should be pressed to encourage a wider teaching of science in the primary schools, so that all children, and not merely those attending secondary schools, might get at least some basic notions of what science is about. It is still more vital to devise methods of reaching the adolescent, whose scientific education (except in the case of those who adopt a scientific profession) stops abruptly with the end of school life. If it could be carried on by the greater use of broadcasting, by a much larger number of public lectures, by science features in the daily and periodical press, by the publication of more popular books on science, and in general by abandonment of the scientist's attitude of aloof silence, we might confidently expect a nation ready to understand and able to use the illimitable resources of mind and matter. It is

idle to expect to capture the adult mind, grown set in its habits of thought, its opinions and its prejudices. On the other hand, to teach the rudiments of science up to the age of 16 and then cease is to waste the harvest of sown seed. The formative process must be continued through the receptive years of early manhood and womanhood, and only scientists can ensure its continuation.

Lastly, if science is to become articulate, it must be taught to walk more closely in step with letters. It is no disparagement to admit that men of science seldom show themselves masters of prose expression. There are of course notable exceptions —the names of DAVY, FARADAY, T. H. HUXLEY, and SIR WILLIAM BRAGG spring at once to the mind—and indeed the chief cause of the taciturnity of science is probably not lack of literary ability but the exacting and engrossing nature of scientific research. The urge to pursue original investigation tends to overshadow the urgency of the public relations of science, so that a task which ought properly to be undertaken by leaders is too commonly relegated to less competent hands. This condition of affairs must be repaired. Science must, in short, learn how to express itself—it must not only accept its responsibility to the public, but acquire the knowledge of how to discharge it.

Correspondence

Contributions and correspondence should be sent to the editor: E. J. Holmyard, M.A., M.Sc., D.Litt., F.I.C., Imperial Chemical Industries, Nobel House, Buckingham Gate, London, S.W.1. Scientists engaged in research of an interesting or important character are invited to send short notes on work in progress and results obtained.

THE FUTURE OF RESEARCH

From J. B. S. Haldane, M.A., F.R.S.

The leading article in the April number of ENDEAVOUR [p. 49] raises a number of important issues. First let me controvert one point. You state that 'In both camps the main and practically sole activity of scientists is directed towards the solution of immediate problems.' This is unfortunately untrue of biologists. Our leaders both in war and industry do not fully realize that the abnormal conditions under which men and women are fighting and working raise enough physiological problems to justify a very large volume of research, some of which would be fruitful at once.

With regard to post-war policy, the writer of the article seems to see no possibilities but either 'the pursuit of knowledge for the sake of knowledge' or its 'application to the amelioration of human existence.' This is a reflexion of the sharp distinction between pure and applied science, between the university and the factory scientist, which characterizes our society. This distinction is not in the nature of things. The founders of the Royal Society were men of intense curiosity, yet they valued 'no knowledge but as it hath a tendency to use.' Large and progressive modern firms allow many of their scientific workers ample opportunities for 'pure' research, and find it pays. In the Soviet Union before the war this tendency had gone very far. Industrial scientists generally did some teaching. Academic research institutions were assigned practical problems, which did not, however, occupy their full time. There was frequent interchange of personnel between laboratories of the different types.

I believe that the best conditions for research, and the happiest for scientists, arise when theory and practice are not separated, but the same man or woman spends part of his or her time with the nose applied to the grindstone of applied science or teaching, and part in the ivory tower of 'pure' research. If the majority of scientific workers would agree that this was a desirable aim, steps might be taken to see that it was realized to some extent at least during post-war reconstruction.

From J. R. Baker, M.A., D.Phil., D.Sc.

British scientists have gladly offered their services to the nation for the period of the war, for use in any way the Government thinks fit. That is right and proper, because modern war is a relatively short-term affair. It is curious to reflect that if this war were likely to last for fifty or a hundred years, the best policy would probably be to leave scientists entirely free to follow their own inclinations. The great technological advances, from the applications of electro-magnetic induction downwards, have nearly always sprung from scientific research carried out by men of genius or talent who wanted to know more about the universe and did not dream of practical results when they were carrying out their work.

Great discoveries are unlikely to be made if after the war we organize science in Britain on totalitarian lines, with the scientific research worker—the only man who counts in discovery —as the lowest term in a hierarchy of planning committees and scientific dictators. As WALTER LIPPMANN has urged in his book *The Good Society*, there is only one thing that can be centrally planned with success, and that one thing is war. Hence the success of totalitarian methods in war should not make us think of totalitarianism as a progressive force in any other sphere.

A growing body of British scientists is

now at last becoming alive to the danger inherent in the demand that science should be centrally planned. One must hope that in the period of reconstruction after the war Britain will maintain her proud position as the champion of liberty not only in the ordinary political sphere, but also over the whole range of human activity, including science and all other branches of culture.

From J. D. Bernal, M.A., F.R.S.

The experience of the war has emphasized, as your April Editorial pointed out, the importance of the organization of scientific effort. There is no reason, however, for the fear that as a result of the experience of the war the development of free science will be curtailed or stunted. Effective organization of science implies neither an exclusive concern with problems of immediate application nor the subjecting of scientists to the discipline of a rigid and unimaginative bureaucracy. Those who have been working for an improvement of the present chaotic system of science in the direction of using it more effectively for human welfare realize fully that any such developments would immediately frustrate their ends. If applied science was exclusively followed, the basic principles on which any new development, however practical, must depend would never be elucidated. It is quite possible for us to see now that, from mathematics to psychology, there is no branch of science that is not needed in one way or another for some application, either now or in the near future.

All branches, therefore, must be cultivated—as they are cultivated, in fact, in the Soviet Union. This does not preclude their cultivation for their own sake by people who enjoy studying them, and even their extensive development on a scale many times that attempted at present even in the countries of the freest science.

Similarly, the planners of science recognize old-fashioned humanistic bureaucracy as an enemy of science. Until a new, scientifically minded bureaucracy can be built up, the organization of science would need to be in the hands of scientists themselves—and not merely of those of senior scientists, but with democratic control that is fully representative of junior scientists and technicians.

Only such democratic organization can secure the real freedom of science, which includes, not only the freedom of discovery, but the freedom to see those discoveries applied. The present freedom of science has reduced the status of the scientist to that of an ineffective dreamer or practical slave to interests far removed from the ideals of science. A free society cannot do without organization—nor can free science.

CHEMISTS AND CHEMISTRY

From E. F. Armstrong, D.Sc., LL.D., F.I.C., F.R.S.

The last war found us largely unprepared as chemists and chemical industry. The lessons were taken seriously to heart, and in 1939, on the outbreak of war, chemists were probably in a better state to meet the emergency than any other section of the community. Two reasons for this were the large and increasing number of highly trained and fully qualified chemists available, thanks to the universities and colleges; and the close co-operation during the last twenty years of the industrial leaders and firms in chemical industry. After all, chemists are the real basic raw material of our industry, and we cannot have too many of them, provided they are of the best. Others should be discouraged at an early stage. The chemist must remember that he gets his first post largely on his teacher's recommendation, but that his future depends on his own ability as a man and a chemist: he has to apply and make useful what he knows.

This war has shown that we are on right lines. There is a need for chemists and chemical engineers if we are to solve the economic problems of the future, and some of us are trying hard to teach the administration and the politicians the truth of the above. But what have we to learn? Surely to be strong in our own house. Every help must be given by firms to the universities so that they have up-to-date and well-equipped laboratories. Some firms already do this generously, but a laboratory is out of date in twenty years, so far more help is needed. Equipment, not endowment, is required. Good workshops and good teachers mean able students and first-class research: a steady flow to a progressive industry.

There are wide fields for our chemical industry to capture. But success is exacting—none but the best will serve to gain it.

JOHN FERGUSON

From John Read, M.A., Sc.D., F.R.S.

I should be obliged if you would record the following bibliographical references originally appended to my article in your January issue (pp. 36 and 37):

[1] J. FERGUSON, *Bibliotheca Chemica*, 2 vols., Glasgow, 1906. [2] *Op. cit.*, **1**, viii. [3] J. J. MANGET, *Bibliotheca Chemica Curiosa*, 2 vols., Geneva, 1702. [4] T. S. PATTERSON, *Annals of Science*, 1937, **2**, 297. [5] T. S. PATTERSON, *Glasgow University Magazine*, 6th December, 1916. [6] F. O. BOWER, *idem*. Without these references, justice is not done to my indebtedness to the quoted writings of Professor T. S. Patterson and Professor F. O. Bower relating to John Ferguson. So far as Professor Patterson is concerned, this indebtedness extends also to the final paragraph of the article. In view of conflicting evidence bearing upon the date of Ferguson's birth, I may add that an official extract from the register of births for the parish of Alloa, kindly sent to me by Mr J. W. Napier, records that 'John, lawful son of Mr William Ferguson and Margaret Kidd,' was born there on 24th January, 1838.

[NOTE: *We regret that very heavy pressure on space in our inaugural issue necessitated omission of this list of references, and are happy now to publish it, together with* PROFESSOR READ'S *interesting addendum.* EDITOR.]

APPLICATIONS OF PHOTOGRAPHY

From George A. Jones

The Association of Scientific Workers is organizing an exhibition which will be held in November at the premises of the Royal Photographic Society. The exhibition is to illustrate the applications of photography to science, medicine, and industry with a view to making such information more generally available and better known to the public. The Photographic Committee of the Association, anxious to obtain examples of such work from as wide a variety of sources as possible, appeals to those who may be able to provide exhibits to write for further details to the Hon. Secretary, Photographic Exhibition Committee, Association of Scientific Workers, 73 High Holborn, London, W.C.1.

The red and blue colouring matters of plants

SIR ROBERT ROBINSON

Aesthetic appreciation of colour is possibly as great among chemists as among artists. But whereas the artist experiences an urge to employ colours, the impulse of the chemist is to probe their chemical composition. Particularly seductive are the red and blue colouring matters of plants, and in the following pages Sir Robert Robinson tells the fascinating story of the way in which he and other workers have mapped the molecular architecture of these complex substances.

The chief groups of vegetable pigments are (*a*) green chlorophyll and its analogues; (*b*) yellow and orange carotenoids, generally insoluble in water and soluble in organic solvents; (*c*) miscellaneous pigments such as those related to anthracene and the colouring matters of fungi; (*d*) the large classes of water-soluble pigments comprising especially the yellow anthoxanthins and the orange, red, magenta, violet, and blue anthocyanins. Our present accurate knowledge of the chemistry of the last group has been gathered since 1913, in which year WILLSTÄTTER and EVEREST published an account of their pioneering researches on cornflower blue. That is not to say that nothing was known previously; indeed, the reactions of the anthocyanins with acids and alkalis were observed by ROBERT BOYLE and NEHEMIAH GREW, and later by many others.

BERZELIUS (1837), MOROT (1850), HEISE (1889), GLAN (1892), and GRIFFITHS (1903) attempted with varying success to isolate the pure pigments, and the results were by no means negligible although the objective was never reached. From the work of Heise and of Glan it appeared that the anthocyanins might be nitrogen-free glucosides. This view was emphasized by the botanist MOLISCH (1905), who showed that anthocyanins sometimes occur in flowers in the crystalline condition and could often be crystallized outside the plant. A well-known experiment of Molisch can be repeated by anyone. Take a few petals of the scarlet pelargonium; roll them on a microscope slide with a glass rod so as to break up the structures. Then add a few drops of acetic acid (80 per cent.), cover with another slide, and set aside for slow evaporation. The acetic acid dissolves out the orange-red pigment and, as the solution concentrates, crystals appear, especially round the edges.

GRAFE (1906–11) carried out a similar process on a larger scale, but unfortunately his examination of this material did not result in any notable advance.

The isolation, characterization, and analysis of many pure anthocyanins were effected by Richard Willstätter and his collaborators (1913–17). The technique varied from case to case, but the standard procedure depended on the recognition that the pigments exist as salts in acid solution. The plant material, usually dried petals of flowers, was extracted with methanolic or ethanolic hydrogen chloride or with acetic acid. The crude pigment salt was precipitated from the solution by addition of a large volume of ether, and this or a similar process might be repeated. The anthocyanin chlorides were then crystallized from aqueous or alcoholic hydrochloric acid. Occasionally a picrate or other derivative was isolated as an intermediate stage in the purification.

In this way the blue or deep bordeaux-coloured cornflowers, the rose, and red dahlias afforded one and the same *cyanin chloride*, which is very sparingly soluble in aqueous hydrochloric acid (0·5 per cent.) and crystallizes in rhombic leaflets or microscopic needles, red by transmitted light and exhibiting a fine bronze lustre. The composition of the crystals is $2C_{27}H_{31}O_{16}Cl$, $5H_2O$, and $C_{27}H_{31}O_{16}Cl$ after drying at 105° C. in a high vacuum. Similarly the scarlet pelargonium afforded a beautifully crystalline (slender, orange-red needles) anthocyanin, $C_{27}H_{31}O_{15}Cl$, termed *pelargonin chloride*.

Complex as the molecules of these colouring matters undoubtedly are, the determination of their molecular structure was made without difficulty except for some details which were finally cleared up by the later syntheses. Boiling 10 per cent. hydrochloric acid brings about a

decomposition by hydrolysis into new coloured salts called *anthocyanidins* and two molecules of glucose:

$$\underset{\textit{Cyanin chloride}}{C_{27}H_{31}O_{16}Cl} + 2H_2O = \underset{\textit{Cyanidin chloride}}{C_{15}H_{11}O_6Cl} + 2\underset{\textit{Glucose}}{C_6H_{12}O_6}$$

$$\underset{\textit{Pelargonin chloride}}{C_{27}H_{31}O_{15}Cl} + 2H_2O = \underset{\textit{Pelargonidin chloride}}{C_{15}H_{11}O_5Cl} + 2\underset{\textit{Glucose}}{C_6H_{12}O_6}$$

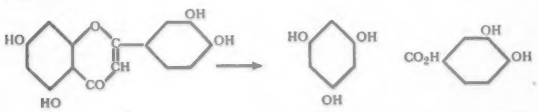
Thus these anthocyanins are diglucosides of the anthocyanidins and the process of decomposition is one with which chemists have long been familiar in the large classes of naturally occurring and synthetic glucosides:

$$C_6H_{11}O_5 - O - R + H_2O \rightarrow C_6H_{12}O_6 + HO{\cdot}R$$

The problem has now been greatly simplified; it is resolved into the recognition of the constitution of the anthocyanidins and the mode of attachment of the glucose molecules to them.

Now cyanidin chloride can easily be made to lose HCl, for example by treatment with aqueous sodium acetate (a weakly alkaline solution), when it yields a deep violet *colour base*, $C_{15}H_{10}O_6$. It could not be overlooked that this is the composition of the anthoxanthin *luteolin*, a yellow mordant dyestuff derived from *Reseda luteola*. The dried plant is called weld and is thought to be the oldest European dyestuff, having been used north of the Alps in the time of JULIUS CAESAR.

Luteolin, which is a typical anthoxanthin (*see above*), forms salts with strong acids, but these are much less stable and far less deeply coloured than cyanidin chloride. Its constitution (I) is known as the result of the labours of A. G. PERKIN and ST. VON KOSTANECKI and the substance has been synthesized by more than one method. A typical decomposition is illustrated and may be brought about by fusion with potassium hydroxide:

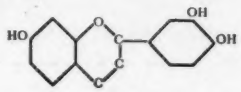


(I) *Phloroglucinol* *Protocatechuic acid*

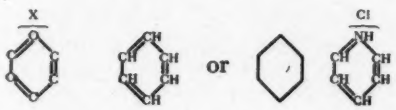
The substance of which luteolin is the tetrahydroxy-derivative is called *flavone* and a large number of variously substituted flavones had already been isolated from plant material.

In order to see whether there is really any relationship between cyanidin and luteolin, Willstätter and Everest fused the former also with potassium hydroxide and were able to isolate phloroglucinol and protocatechuic acid. It then seemed highly probable that cyanidin chloride contained the group (II).

Another series of researches, tending to confirm the deduction, concerned the constitution of the best-known group of relatively stable oxonium salts, so called by analogy with ammonium salts. Through the researches of COLLIE, BAEYER, WERNER, DECKER and FELLENBERG, and W. H. PERKIN and ROBINSON, it was already known that these invariably contain a structure known as pyrylium (III), which may be compared with benzene (IV) and pyridine hydrochloride (V):

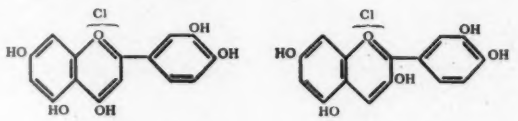


(II)



(III) (IV) (V)

Thus, in harmony with the pyrylium theory, luteolin hydrochloride would be (VI), and since the products of decomposition forbid us from suggesting modification of the benzene rings, the only possible cyanidin structure closely related to luteolin is (VII):

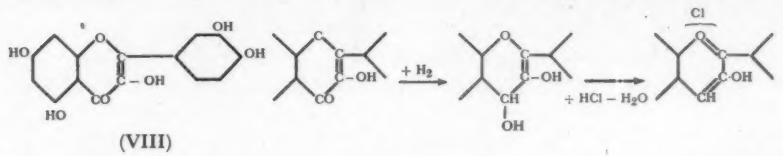


(VI) (VII)

[The bracket in these formulae indicates the electrovalency of salts as in $\overset{+}{Na}\}\overset{-}{Cl}$ or $\overset{+}{NH_4}\}\overset{-}{Cl}$ where charged ions are bound by electrostatic attraction. Such valency differs from the type represented by lines and exemplified by that in the hydrogen molecule, $H \overset{\times}{\times} H$, which is non-polar (co-valency), the binding force depending on sharing of electrons between two atoms.]

The formula (VII) indicates that cyanidin chloride might be related also to the most widely distributed of all anthoxanthins, namely quercetin (VIII), and a rigid proof of the fundamental structure of the anthocyanidin was obtained when it was found that it could actually be produced by reduction of quercetin in acid solution. The reagent was magnesium in methanolic hydrochloric acid solution, and the fact that the yield was poor does not invalidate the experiment. The changes in the centre nucleus are shown in

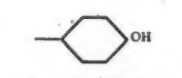
part formulae and they accord with analogies in other series:



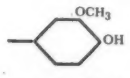
(VIII)

That (VII) correctly represents cyanidin chloride was later proved by several unambiguous syntheses, and moreover all the known anthocyanidins have been synthesized, as well as some hundreds of similar pyrylium salts. The only differences between them lie in the number, nature, and positions of the groups attached to the triple ring system.

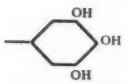
Later Willstätter and his co-workers isolated other anthocyanins. Delphinin chloride from delphinium flowers splits up into *delphinidin chloride*, $C_{15}H_{11}O_7Cl$, two molecules of glucose, and two molecules of *p*-hydroxybenzoic acid. The true analogue of cyanin and pelargonin based on delphinidin is *delphin chloride*, $C_{27}H_{31}O_{17}Cl$, and this was later isolated by SCOTT-MONCRIEFF and ROBINSON from flowers of *Salvia patens*. Anthocyanidins, which are methyl ethers of cyanidin and delphinidin, were also obtained by hydrolysis of various anthocyanins. Except in one case the variations are all in the right-hand nucleus and therefore this alone need be represented. As already stated, all have been synthetically prepared.



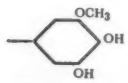
Pelargonidin chloride



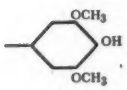
Peonidin chloride



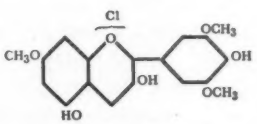
Delphinidin chloride



Petunidin chloride



Malvidin chloride

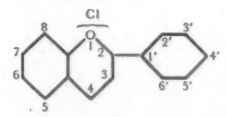


Hirsutidin chloride

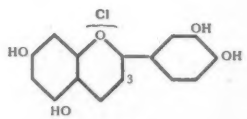
The most widely distributed are pelargonidin, cyanidin, delphinidin, and malvidin; hirsutidin occurs only in certain primulae.

The red poppy (*Papaver rhoeas*) is coloured by mecocyanin, an isomeride of cyanin chloride and also a diglucoside of cyanidin. Many monoglucosides are known, a few monogalactosides and many rhamnoglucosides and pentoseglucosides. A very common occurrence is acylation of a number of hydroxyl groups as in delphinin chloride. *Callistephin* from the aster (Willstätter) or the red carnation (Robinson) is pelargonidin monoglucoside. *Chrysanthemin* from the deep red chrysanthemum is cyanidin monoglucoside; *oenin* from the skins of purple-black grapes is malvidin monoglucoside; the monoglucoside of peonidin occurs in the skins of the larger cranberries from Newfoundland. Cyanidin monogalactoside colours the smaller European cranberries; it is called *idaein;* the red snapdragon (*Antirrhinum majus*) contains *antirrhinin*, which is cyanidin rhamnoglucoside. These examples will suffice to indicate the range of anthocyanins, but many other types are known.

The problem of the point or points of attachment of the sugar residues remains and this has been solved by three methods: in a very few cases by degradation (KARRER), by comparisons of properties with anthocyanidins of known structure synthesized for the purpose (Robinson and coworkers), and later by total synthesis of the anthocyanins themselves. As an example of the second method, cyanidin chloride dissolves in aqueous sodium carbonate to a pure blue solution, but chrysanthemin gives a violet-coloured solution that becomes blue on the addition of sodium hydroxide. The sugar residue in the monoglucoside covers up one hydroxyl group and so modifies the reactions; the question is, which hydroxyl group is concerned?



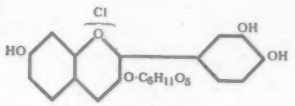
Numbering scheme



(IX)

We know from a different reaction that hydroxyls in positions 3′ and 4′ are free. Cyanidin chloride in weakly acid solution gives a very intense blue coloration on the addition of a trace of a ferric salt. This behaviour is shown only by synthetical anthocyanidins which have two hydroxyl groups in neighbouring (*ortho*) positions in the benzene ring. Chrysanthemin exhibits this ferric reaction and therefore the sugar is not attached to position 3′ or to 4′. When anthocyanidins containing one hydroxyl less than cyanidin were synthesized it was found that only

(IX) behaved like chrysanthemin towards alkalis; hence it became very likely that the hydroxyl in position 3 is not free in this monoglucoside. In other words, the indication was that chrysanthemin is cyanidin 3-monoglucoside (X). The probability was greatly increased when it was found



(X)

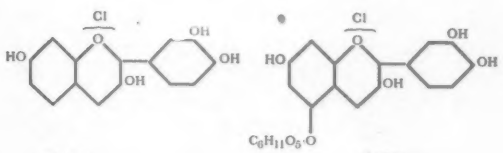
by similar comparisons that *all* the monoglucosidic anthocyanins should be anthocyanidin 3-glucosides.

It has been mentioned above that mecocyanin chloride is isomeric with cyanin chloride, and it is noteworthy that the behaviour of the two pigments in solutions of varying *p*H is quite different. The reactions of mecocyanin are, in point of fact, almost identical with those of chrysanthemin. Very careful hydrolysis splits mecocyanin into chrysanthemin and glucose and the pigment is accordingly chrysanthemin glucoside. As we know from the study of a large variety of synthetical pyrylium salts of known constitution that the properties in question are evidence that only one hydroxyl of cyanidin (in position 3) can be modified, it follows that mecocyanin should be a bioside and contain the group

$$-O\cdot C_6H_{10}O_4\cdot O\cdot C_6H_{11}O_5$$

in position 3. This hypothesis was justified by synthesis (*see below*), and a similar argument applies to antirrhinin, which is cyanidin 3-rhamnoglucoside.

But cyanin chloride is evidently something different, and at first we thought it must be cyanidin 5-bioside because the salt (XI) gives colour reactions similar to those of cyanin. This seemed to be confirmed when the part-hydrolysis of cyanin was found to give a new cyanidin monoglucoside called cyanenin and this could only be cyanidin 5-glucoside (XII).



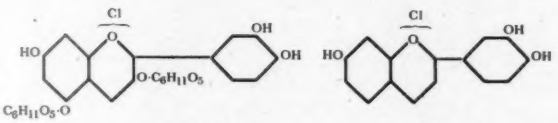
(XI) (XII)

Again this latter view was proved to be correct by synthesis.

Closer study disclosed a new touchstone and a definite difference in behaviour between cyanenin and cyanin.

A very dilute acid solution of an anthocyanin cannot be preserved indefinitely in contact with air; the pigment is destroyed by oxidation. The process is hastened by the presence of catalysts such as iron salts, and it was noticed that the natural anthocyanins are far more stable in this respect than the anthocyanidins derived from them.

Using standardized conditions, including the addition of a minute relative amount of ferric chloride, it was found that the pigments could be divided into two classes: one group slowly destroyed during many hours, the other quickly destroyed in a few minutes. The substances of known structure in the former class contained no free hydroxyl in position 3, whereas this group was present in the substances of the latter class. Cyanenin (like cyanidin) was quickly destroyed, but cyanin (like chrysanthemin and mecocyanin) was very stable towards such aerial oxidation. The logical conclusion was that cyanin must be a 3-glucoside, and since it is also a 5-glucoside it should be cyanidin 3 : 5-dimonoglucoside (XIII). Then it was found that the colour reactions of (XIV) were like those of cyanin.



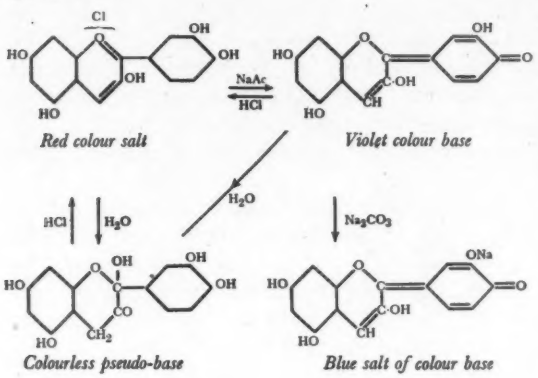
(XIII) (XIV)

The correctness of this line of argument was eventually proved by synthesis, and similar methods showed that pelargonin, malvin (from *Malva sylvestris*, certain *Primulae*, and later many other natural sources), delphin, petunin (from petunias), and hirsutin (from *Primula hirsuta*) are also 3 : 5-dimonoglucosides of the respective anthocyanidins. In the case of pelargonidin derivatives, modification or elimination of the hydroxyl in position 5 is recognized by the exhibition of a yellow-green fluorescence in acid alcoholic solution. Pelargonidin and callistephin show no fluorescence, but pelargonin and pelargonenin (pelargonidin 5-glucoside obtained by part-hydrolysis of pelargonin) fluoresce brightly.

CHEMICAL BASIS OF COLOUR REACTIONS

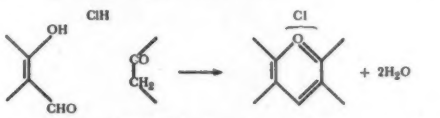
In dilute faintly acid solution the anthocyanidins and anthocyanins are often converted into colourless *pseudo-bases* from which they may be

regenerated by the addition of acid. The changes in solution may be represented in the case of cyanidin:

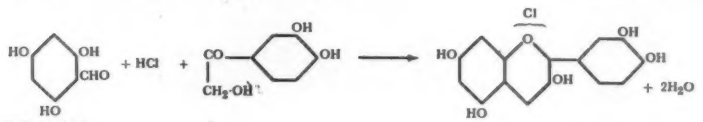


SYNTHESIS OF THE ANTHOCYANINS

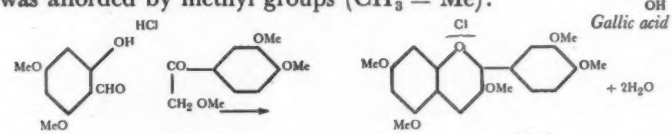
The method employed was an elaboration of a pyrylium salt synthesis discovered independently and simultaneously by Decker and Fellenberg and W. H. Perkin and the writer in 1907. A suitable hydroxyaldehyde is condensed with a substance containing the group $-CO-CH_2-$ by means of hydrogen chloride:



Thus we might expect to be able to synthesize cyanidin chloride as shown below:



Phloroglucinaldehyde is a well-known substance, but when it is touched with hydrogen chloride it begins to condense with itself, and this process occurs more rapidly than the desired synthesis, so that phloroglucinaldehyde cannot be employed. In all such cases the organic chemist employs the device of protecting the reactive (or activating) groups, as in the familiar example of the industrial preparation of *p*-nitraniline. In the earlier work this was overdone and full protection was afforded by methyl groups (CH_3 = Me):



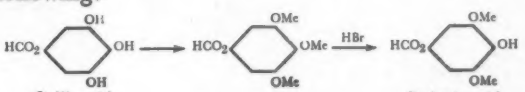
(XV)

This O-pentamethylcyanidin chloride (XV) was converted into cyanidin iodide by boiling concentrated hydriodic acid. The iodide was transformed into the chloride by means of silver chloride and the product shown to be identical with cyanidin chloride from cyanin and chrysanthemin. Pelargonidin and delphinidin were synthesized in a similar fashion, but it is obvious that partly methylated anthocyanidins such as malvidin could not be obtained in this way. The process used for the removal of the methyl groups was too vigorous and non-selective.

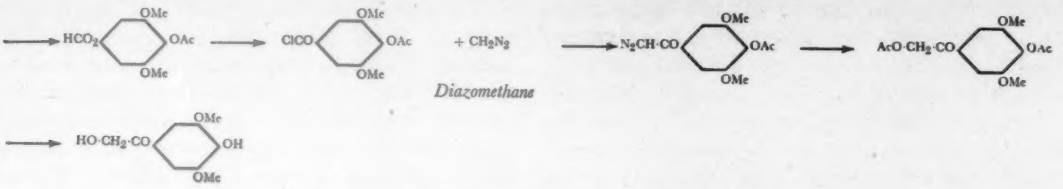
After considerable experimentation it was found that one benzoyl group is sufficient protection for the phloroglucinaldehyde, whilst the second component need not be protected at all. The resulting benzoylanthocyanidins can be hydrolysed by cold aqueous alcoholic sodium hydroxide, which also breaks open the central ring. Addition of hydrochloric acid reconstitutes the ring and provides the anthocyanidin. All the anthocyanidins have been synthesized in this way, the chief problem being the preparation of the appropriate second components.

Taking no account of the synthesis of the benzoyl group, benzoylphloroglucinaldehyde can be made from carbon in ten stages: $C \rightarrow CaC_2 \rightarrow C_2H_2 \rightarrow C_6H_6 \rightarrow C_6H_5NO_2 \rightarrow C_6H_4(NO_2)_2 \rightarrow C_6H_3(NO_2)_3 \rightarrow C_6H_3(NH_2)_3 \rightarrow C_6H_3(OH)_3 \rightarrow C_6H_2(OH)_3CHO \rightarrow C_6H_2(OH)_2(O{\cdot}COC_6H_5)CHO$. In the laboratory we start from purchased phloroglucinol, probably made by the above method from coal-tar benzene (C_6H_6). Our second starting-point in the case of malvidin is gallic acid, always prepared by the hydrolysis of naturally occurring tannin. It may be made from carbon by the eight stages: $C \rightarrow CaC_2 \rightarrow C_2H_2 \rightarrow C_6H_6 \rightarrow C_6H_5SO_3H \rightarrow C_6H_5OH \rightarrow C_6H_4(OH)CO_2H \rightarrow C_6H_2Br_2(OH){\cdot}CO_2H \rightarrow C_6H_2(OH)_3{\cdot}CO_2H$, in which the formation of sodium salts and acids from them is disregarded.

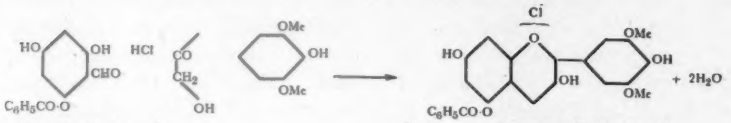
The remaining steps from gallic acid are the following:

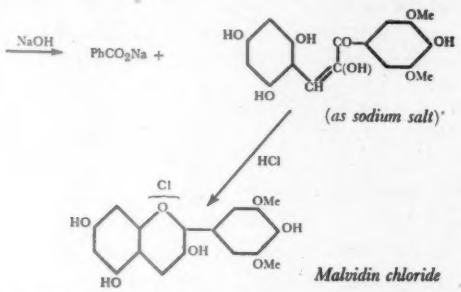


[This last step is a selective part-demethylation and the correctness of the constitution assigned to syringic acid has been rigorously proved.]

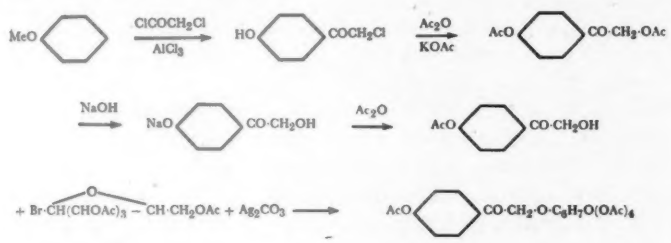


The synthesis succeeds in ethyl acetate solution in the cold:

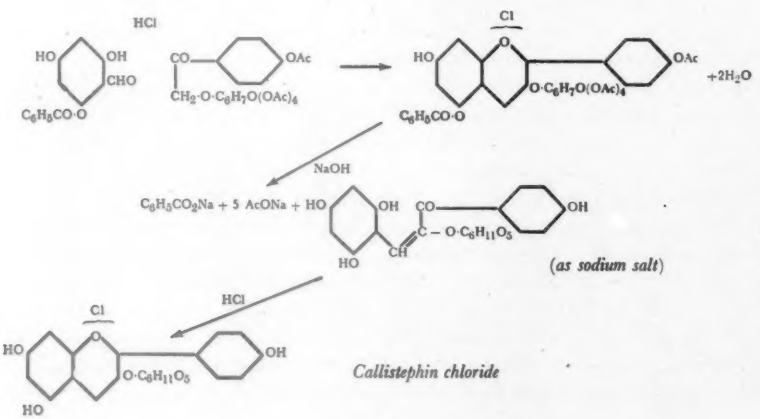




In applying such methods to the anthocyanins themselves, formidable experimental difficulties had to be surmounted because of the ease with which glucosides are hydrolysed by hydrochloric acid in the high concentration that must be employed. The preparation of the glucosidic components also presented obstacles, especially in the delphinidin and methylated delphinidin series. The simplest example is that of callistephin:

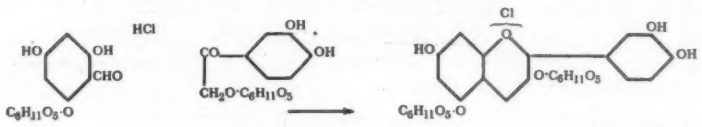


Then



Similarly, by putting the glucose in the right places, the three other pelargonidin monoglucosides were synthesized and the work was extended to cover the whole field. The naturally occurring anthocyanins that have been artificially prepared are callistephin, pelargonidin 3-galactoside (which occurs in strawberries), chrysanthemin, idaein, delphinidin 3 - monoglucoside (in hydrangea flowers), delphinidin 3-monogalactoside, oenin, malvidin 3-monogalactoside, mecocyanin (which proved to be cyanidin 3-gentiobioside; the cellobioside, lactoside, and maltoside were made for comparison), antirrhinin (unpublished work), pelargonin, cyanin, delphin, and malvin.

It was later found that cyanin could be directly synthesized from unprotected components as below, but it is better to use the standard method:



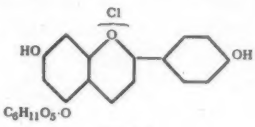
Cyanin chloride

A SURVEY OF ANTHOCYANINS

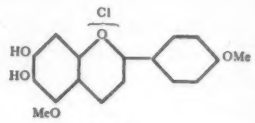
The possession of pure specimens of the chief anthocyanins enabled us to compare their reactions with those of solutions made by extracting plant material with 1 per cent. hydrochloric acid, and to devise procedure for the rapid examination of such extracts. Thus the anthocyanins present in a large number of species and varieties have been recognized, only a few flower petals or leaves being needed for the purpose. Substances known as co-pigments modify the colour reactions and other properties of the anthocyanins, but these disturbing influences can often be removed or, if not, allowance may be made for them. The chief co-pigments are tannins and anthoxanthins. A great variety of quick tests is available and these are applied both to the anthocyanin and the derived anthocyanidin. They include colour in acid solution in water and alcohol, colour reactions with sodium acetate, sodium carbonate, sodium hydroxide, the ferric reaction, a destructive oxidation test in about 5 per cent. sodium hydroxide, various special tests, and above all examination of the distribution ratios between 1 per cent. hydrochloric acid and immiscible organic solvents.

The use of amyl alcohol for this purpose was introduced by Willstätter. Anthocyanidins are completely extracted by this solvent from aqueous solution. Monoglucosides have distribution numbers (percentage of pigment that passes to the amyl alcohol under standard conditions) from 9 to 50, while diglucosides have low distribution numbers, from nearly zero to about 5. The method may be used for separation and purification purposes. Thus an anthocyanidin may be returned to 1 per cent. hydrochloric acid from an amyl alcoholic solution by the addition of benzene or light petroleum. Then it can be taken up again in amyl alcohol and so 'shuttlecocked' between the solvents until a sufficient degree of purity has been attained. Special mixtures have been devised for the purpose of differentiating the anthocyanidins. One mixture extracts much pelargonidin and peonidin, a little cyanidin, but no delphinidin, malvidin, or petunidin. Another extracts all the pelargonidin, peonidin, and malvidin, about half the cyanidin, some petunidin, and no delphinidin. Distribution methods also allow us to distinguish monoglucosides from rhamnoglucosides and these again from diglucosides.

As a result of this extensive survey only a few really novel types have come to light. The orange-red flowers of *Gesnera fulgens* contain gesnerin (XVI as chloride) which was synthesized for comparison. It is the only known anthocyanin not bearing oxygen in position 3:



(XVI)



(XVII)

A similar substance is *carajurin* (XVII, as hydrochloride), which was isolated from a rare cosmetic pigment used by the Indians of the Orinoco (A. G. PERKIN, CHAPMAN, and the writer, 1927). From what little we know of the method of preparation it is likely that it occurs in the plant, probably a *Bignonia*, in the form of a glucoside.

Various anthocyanins not yet isolated in substance have been recognized in plant material; for example, a pelargonidin 3-bioside occurs in the orange-red nasturtium flowers and a pelargonidin 3-rhamnoglucoside in the scarlet gloxinia.

Entirely new unidentified anthocyanins, as well as some of the types found in flowering plants, colour the young fronds of ferns; gymnosperms also have the power of producing these colouring matters. The point of entry into the vegetable kingdom has not yet been exactly located; in spite of statements to the contrary these pigments have

not been found in bacteria, nor, so far as the writer is aware, in algae or fungi.

They may occur in almost all parts of plants: roots, stems, leaves, sepals, fruits, and flowers. The colour may be permanent, as in leaves of *Coleus*, or transitory, as in growing root-tips of certain saxifrages and in many young leaves. This wide distribution suggests a definite physiological function which, however, has not been elucidated. It may be protective (anti-oxidant?), but no satisfactory evidence of its nature has yet been garnered. Anthocyanins frequently appear at the site of injury of a plant, and autumnal reddening of leaves is another manifestation of these substances.

There is an overwhelming preponderance of cyanidin derivatives in young leaves, wound-anthocyanins, and in autumnally reddened leaves, and there is good statistical evidence that cyanidin may be regarded as the normal type. Pelargonidin requires a stage of reduction and delphinidin a stage of oxidation. It has been shown that the state of oxidation of the aromatic nuclei in cyanidin is the natural result of the theory that the substance is built up in the plant according to the scheme:

$C_6 + C_3 \rightarrow C_6 - C_3 + C_6 \rightarrow C_6 - C_3 - C_6$

Numerous representatives of the $C_6 - C_3$ types postulated as intermediates are known among natural products.

Flowers, especially garden flowers, are more highly specialized, and in them the anthocyanins have been differentiated and evolved to accommodate the requirements of reproduction (attraction of insects), climate, and horticulturists. Red flowers predominate in tropical regions and many are based on pelargonidin; even when delphinidin occurs the flower is often red. On the other hand, the higher alpine flora is characterized by a majority of blue flowers based on delphinidin.

Even so, cyanidin holds its own among the colours of flowers of all types. Of 530 species examined, 19 per cent. contain pelargonidin derivatives, 40 per cent. contain cyanidin or peonidin derivatives, and 50 per cent. contain delphinidin, malvidin, petunidin or hirsutidin derivatives. Of the 299 genera examined, 52 per cent. contained cyanidin derivatives. In families the percentage of cyanidin derivatives was 72, and in orders 80. This shows clearly the effect of differentiation; it should be noted that the more accessible and brightest flowers have naturally been studied first, and it is just these which have been most highly specialized.

NITROGENOUS ANTHOCYANINS

WILLSTÄTTER and SCHUDEL made a preliminary examination of betanin, the colouring matter of the beet, and showed that it contained nitrogen. Subsequently bracts of bougainvillaea afforded another member of the series (PRICE and the writer). Little is known of the chemistry of these pigments, but they are glucosides and their characteristic properties have been simulated by synthetical compounds containing an amino-group in the usual anthocyanidin molecule. The compositions of betanin and bougainvillaedin suggest that the anthocyanin molecule is attached to the amino-group of a protein amino-acid. Nudicaulin (PRICE, SCOTT-MONCRIEFF, and the writer), the yellow colouring matter of the Iceland poppy, also contains nitrogen and seems to be related to the group.

Nitrogenous anthocyanins have been found in five orders only, namely *Caryophyllales*, *Chenopodiales*, *Lythrales*, *Thymeleales*, and *Cactales*. It is probable, therefore, that the *Cactales* are not so remote from the four orders first named as is tentatively suggested by HUTCHINSON in his *Families of Flowering Plants* (1926).

NATURALLY OCCURRING SUBSTANCES RELATED TO ANTHOCYANINS

The anthoxanthins of the flavone (e.g. luteolin) and flavonol (e.g. quercetin) classes have already been mentioned. They occur in the plants as glucosides and represent an oxidized form of the central nucleus. There is no evidence that they are obtained from the anthocyanins by oxidation or that they are reduced *in vivo* to anthocyanins. Much more probably they are derived from common precursors by a forking of the roads. There is greater variety of constitution among the anthoxanthins than among the anthocyanins, and the two classes occurring together are more often than not unrelated.

It need occasion no surprise that the most common anthoxanthin, quercetin, is found alongside the most common anthocyanidin. It would be strange if this concurrence were not observed in a few cases, and the fact is not so significant as it would be if the types found together were uncommon.

More reduced substances are the leucoanthocyanins, the catechins, cyanomaclurin, peltogynol, etc. The term *leucoanthocyanin* has been used to denote very widely distributed substances that afford anthocyanidins when treated in air with hot alcoholic hydrochloric acid. There is little

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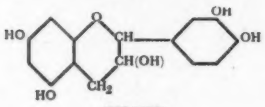
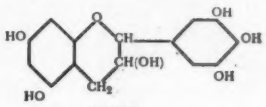
doubt that these are closely related to the anthocyanins and may be sources of the pigments under certain circumstances. That they are normal precursors is highly improbable. Some leucoanthocyanins give rise to pelargonidin and some to delphinidin, but the great majority give rise to cyanidin.

Catechins (XVIII), (XIX) represent the most reduced form of the anthoxanthin-anthocyanin types and APPEL and the writer have been able to oxidize Gambier-catechin (XVIII) to cyanidin. The process was indirect and involved methylation, oxidation by bromine to a methylated bromo-cyanidin, and then combined demethylation and elimination of bromine under the influence of hot hydriodic acid. This is perhaps the easiest way to acquire a supply of cyanidin:



(XVIII)



(XIX)

GENETICS OF FLOWER COLOUR

Only a brief reference to this subject can be made since it demands separate treatment. The methods developed for the purposes of the survey of anthocyanins have been found invaluable in making the large number of analyses required in connexion with breeding experiments.

The genes responsible for variations of flower colour have been identified in many genera, and some important deductions have been drawn in regard to the mechanism of anthocyanin synthesis in the plant. For example, a study of *Dahlia* by LAWRENCE and SCOTT-MONCRIEFF has made it very probable that the anthocyanins and anthoxanthins are derived from two common precursors, one of which is plentiful and the other in limited supply.

The writer and LADY ROBINSON have been privileged to participate in one of these investigations, namely that on Sweet Peas (BEALE, ROBINSON, ROBINSON and SCOTT-MONCRIEFF). The figures opposite, reprinted from the *Journal of Genetics* (1939), illustrate some of the main types and incidentally form an epitome of the causes of variation of flower colours. The larger part of the flower is called the standard and the lower smaller section represents the wings.

(1) Purple, hooded, dark wing. The anthocyanin is based on delphinidin; it is diglucosidic and methylated (petunidin and malvidin).

(2) Red, hooded, dark wing. Anthocyanin based on cyanidin and largely peonidin diglucoside.

(3) Salmon, hooded, dark wing. Anthocyanin, pelargonidin diglucoside.

These three illustrate differences due to the nature of the anthocyanin.

(4) Purple, light wing. Anthocyanin as in (1), but much co-pigment and little anthocyanin in the wings.

(5) Copper or maroon, standard and wings identical, no co-pigment present in wings. This type is found in purple, red, and salmon flowers, the example given being based on delphinidin. The absence of co-pigment is associated with ready bleaching in sunlight and is due to a specific gene.

(6) Mauve, hooded, dark wing. Anthocyanin based on delphinidin. Much co-pigment and little anthocyanin throughout.

(7) Purple, dark wing. Anthocyanin based on delphinidin, co-pigment in wings.

(8) Dull, dark wing. As (7) but the cell-sap has a higher *p*H (more alkaline).

(9) Red, dark wing. As (2) but lacking factor H (hooded) and co-pigmented in the wings.

(10) Dull red, dark wing. As (9) but the cell-sap has a higher *p*H.

It should be noted that many factors, e.g. 'hooded', are associated with changes in anthocyanin concentration, in this example with an increased content. Thus (1) and (2) contain relatively more anthocyanin than (7) and (8) and (9) and (10) respectively.

The writer cannot close without acknowledging his deep debt to enthusiastic collaborators, among whom DRS D. G. PRATT and W. BRADLEY, PROFESSORS A. ROBERTSON and A. R. TODD, must be specially mentioned in connexion with synthetic work. LADY ROBINSON took a leading part in the survey of anthocyanins and leucoanthocyanins and MISS R. SCOTT-MONCRIEFF (MRS MEARES) has been a pioneer in the field of genetics of flower colour. DR J. R. PRICE worked on nitrogenous anthocyanins and has notably extended the survey.

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The substance of heredity

C. D. DARLINGTON

'Like father, like son'—but why and how? Scientists have long had some inkling of the general mechanism of heredity, but during the last few years a wealth of detailed and precise information on the subject has been acquired. Dr Darlington here reviews recent work and shows that the transmission of hereditary characters is ultimately a chemical process.

Perhaps the simplest, and the earliest, view of heredity is that of a *force*, a force which interacts with that of the environment to give the organism as we know it. The effectiveness of this force is expressed in the proverb that you cannot make a silk purse out of a sow's ear. A second view, likewise early and originally simple, is that heredity is a *law*, the law that like begets like. Both these views find their place in recent genetics. The first appears as JOHANNSEN'S formal and perhaps mystical concept of the genotype interacting with the environment to give the phenotype or visible character. The second appears as MENDEL'S laws of segregation and recombination. But there has been a third view of heredity derived not from popular belief but from philosophy, namely that heredity is a *substance:* that its force and its laws are merely the properties of the *genitalia corpora* of the Greek materialists. It is to this last view that genetics has come in the last twenty years. The substance is the chromosomes, the laws are the mechanics, and the force is the chemistry of these bodies.

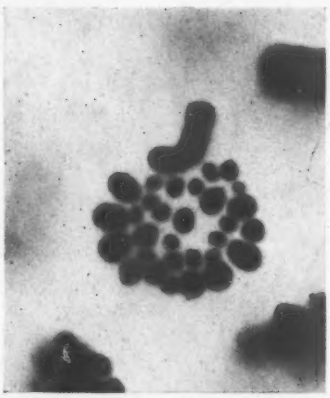


FIGURE 1 – *Chromosomes at mitosis in a male grasshopper,* Leptophyes punctatissima. *There are thirty ordinary chromosomes, and one X chromosome at the top.* (× 2,400)

What, then, are chromosomes? To understand them we must recall that the whole body of the plant or animal is divided into compartments or cells, each of which contains a living unit. Blood-corpuscles, pollen grains and eggs are easily separated cells, whereas tissues like muscle and brain are masses of cells closely bound together. Each of these cells is governed by a small globular body which we call the nucleus. As the plant or animal grows its cells divide, and this division or mitosis naturally entails the division of the nucleus. When the nucleus divides it resolves itself into a number—constant for any particular individual—of rod-shaped bodies which are the chromosomes (figure 1).

Every cell in the body keeps its fixed number of chromosomes because when the nucleus divides each of the chromosomes splits lengthwise and its identical halves pass to the opposite daughter-cells. Here we begin to see the mechanism of heredity at work, since this process of division maintains complete uniformity in the controlling substance of heredity throughout the body.

The number of chromosomes is not only uniform. It is usually even. The meaning of this becomes clear when we watch the formation of the germ-cells—eggs and spermatozoa. In the parent-cell, which divides to give the germ-cells, the chromosomes associate in pairs, and by tracing their history backwards we can prove that one member of each of these pairs is derived from the mother and one from the father. Every plant or animal therefore has a double heredity. Furthermore, the partners separate without themselves dividing, so that the eggs and sperm get only half the number of chromosomes: the *diploid* number, as we say, is reduced to the *haploid*. And when the egg is fertilized by the sperm a new individual is created with the diploid number again.

This individual is new in an hereditary or genetic sense because it has a new combination of chromosomes different from that of either of its parents. Indeed, since each pair of chromosomes can break and recombine, or 'cross over' at many places, and at different places in different parent-cells, each of the progeny is likely to be different from every one of its brothers or sisters (figure 2).

Let us see how this shows itself in practice.

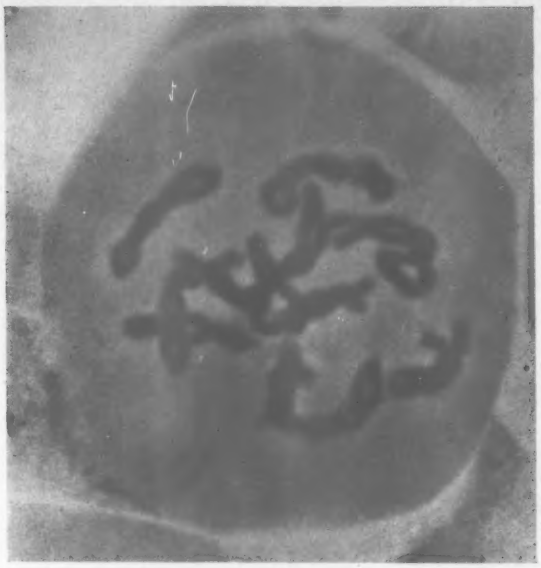


FIGURE 2 – *Twelve paired chromosomes in a pollen mother-cell of a lily*, Fritillaria chitralensis. *The points where the loops meet mark the positions of crossing over between the partners.* (× 1,600)

Most hereditary differences, such as height and skin colour in man, are determined by the interaction of all the chromosomes, which differ in many minute respects. But often we have large and simple differences. These were the ones BATESON used in his pioneer work on the breeding of poultry. He found that black and white breeds crossed together gave either black, 'blue,' or white progeny. But when a second generation was raised by crossing two blues they would never breed true. They always produced black, blue, and white in the proportions of 1 : 2 : 1. There was a clean separation or segregation of the three types. When Mendel had first obtained this kind of result he supposed that the first generation had mixed hereditary factors *Bb* (black—white). It therefore formed equal numbers of germ-cells with *B* and *b* and gave progeny with the factor combinations *BB : Bb : bb* in the proportions 1 : 2 : 1. Now we can see that the chromosomes exactly fulfil these conditions by their pairing and division in the germ mother-cells.

One of the most important hereditary differences is that of sex itself, and since the segregation is so sharp and the ratio of approximate equality between males and females so general, it is natural to suppose that here we have a single hereditary difference. For example, if females were all *XX* and males all *Xx*, then the progeny from the inevitable cross *XX* by *Xx* would be half of each sex. In fact, we find that all mammals have a pair of chromosomes which we call *XX*, or the sex chromosomes, in the females, while in the males there is only one *X*, which pairs with a very small partner differing from the large *X* in simply lacking about half its length. The little one we call *Y*. The male is a male because he has less heredity [6]. This is even clearer in many insects where there is no *Y* chromosome at all and the male is just one chromosome short (figure 1).

This system of sex determination has some striking consequences in heredity. Take the tortoiseshell cat. She has a strange tale to tell. To begin with, she is always a female. When she is crossed with either a black or a yellow tom, her male offspring are black and yellow in equal numbers. The father makes no difference. Clearly the tortoiseshell is mixed for black and yellow, and the factors or *genes* for black and yellow lie in the *X* chromosome and not in the *Y*. The male therefore cannot have the mixed heredity necessary for the tortoiseshell patching.

What makes one gene determine the black colour while its alternative determines the yellow? We cannot yet give the answer, but in trying to give it we have gone some way towards understanding the chemistry of the chromosomes and the genes.

To begin from the inside. We find the chromosome consists of a protein fibre not entirely unlike hair or silk [1]. It depends on the peptide chain linkage —C—C—N—. On this framework are fixed at intervals the active groups which we know as genes. The genes regulate amongst other things the division cycle of the nucleus, and this they do by a very definite and uniform chemical device in all organisms. They attach to themselves series of flat plates, the nucleotides of thymonucleic acid, which polymerize in columns parallel with the slender polypeptide fibres. The plates are spaced at exactly the same distance apart as the atoms in the peptide chain—3·4 Ångström units, as ASTBURY found from X-ray analysis (cf. this Journal, Vol. I, pp. 70–73). These well-fitting columns are responsible for the two primary properties of chromosomes and genes, namely coiling and reproduction. The coiling of the chromosome is what enables it to contract from the fine dispersed thread of the working nucleus to the rod which manœuvres itself into position for regular distribution when the cell

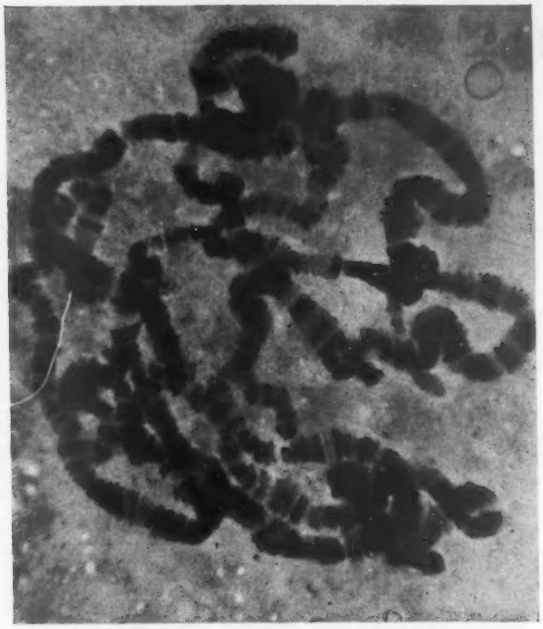


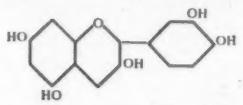
FIGURE 3 – *Resting nucleus of a salivary gland cell in the fly* Drosophila melanogaster. *The genes have undergone eight cycles of reproduction and so occur as series of flat plates each with* 256 *genes. The larger genes make deeper staining bands.* (× 1,500)

divides. The reproduction is the basis of heredity, and indeed of life, for without identical reduplication any living system would quickly break down (figure 3).

Nucleic acid renders a further invaluable service—it makes the chromosomes visible. This it does in two ways: by absorbing dyes differentially and also by absorbing ultra-violet light differentially, a method of study developed by CASPERSSON (cf. [2]), figure 4. We can therefore very easily see what is happening to the nucleic acid. We find that some parts of the chromosomes throw off their coat of nucleic acid when they re-form the nucleus at the end of the cell-division. It is then stored in a special body, the nucleolus, and in a special reserve form with a different sugar radicle. Other parts do not (figure 5), and these we find are the parts that are doing no work in the cells in question. There are some blocks of genes, or even whole chromosomes, that rarely seem to work, and we find that such blocks can be broken off by X-rays, or otherwise lost, without the organism being much the worse for it. If we enable cells with such inert chromosomes to divide at freezing-point we see these chromosomes in a starved condition. They are starved of nucleic acid and the gene string of the chromosome is naked and almost unstained (figure 6). In extreme cases it then fails to coil and to reproduce properly [3].

Here we see a little of how the machinery of heredity works from the inside. From the outside, the task of inquiry is bigger, more laborious, and more elaborate. A few instances will show how the problem is being tackled (cf. [5]).

The chief flower colours rest on a basis of red and blue pigments, the anthocyanins, whose detailed structure and variations have recently been revealed by ROBINSON at Oxford (see p. 92). The simplest of these pigments is a glycoside of cyanidin which is the usual basis of leaf and stem colours and seems to be derived from two hexose units and one triose arranged as follows:



The great variety of flower pigments has apparently been developed from this basic type by oxidation, reduction, methylation, and addition of a second sugar radicle, at various positions. Each of these changes can be determined in the plant by the mutation of a single gene. Study of the effects of combinations of different genes in various plants has enabled LAWRENCE and PRICE [7] to work out the order in which the several genes act during the process of formation of these pigments from sugar in the cell. Their work supports the view that the products of the different genes interact during development sometimes by co-operation, sometimes by competition, sometimes even by interference, and that by determining in this way one another's activity or

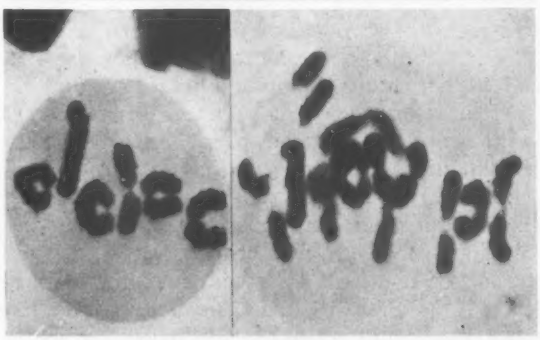


FIGURE 4 – *Paired chromosomes in pollen mother-cells of two species of* Tradescantia. *Right: six pairs in a cell fixed and stained in acetic orcein. Left: twelve pairs in a living cell photographed with ultra-violet light.* (× 1,000)

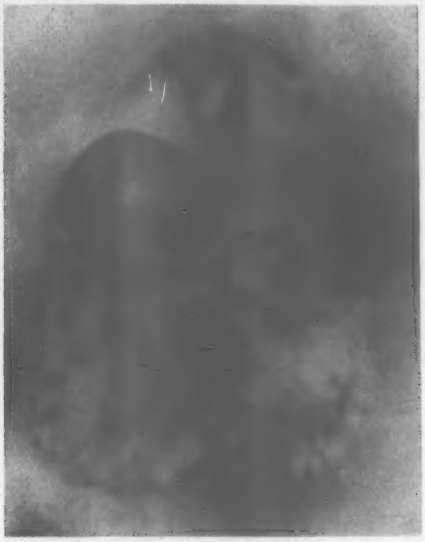


FIGURE 5 – *Embryo-sac mother-cell of* Fritillaria pudica *showing three condensed masses of inert chromosome charged with thymo- or desoxyribose-nucleic acid and the large faintly stained sphere containing the reserve of ribose-nucleic acid. The differentiation is produced by Feulgen's staining method which depends on Schiff's aldehyde reaction.* (× 2,400)

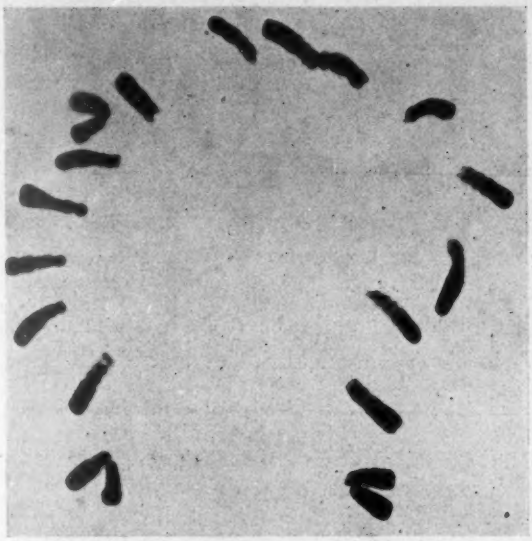


FIGURE 6 – *Starved chromosomes reduced by cold treatment in the pollen grains of* Fritillaria pudica. *The pale bands are inert segments.* (× 1,800)

inactivity they jointly regulate the whole process of development.

Most gene differences depend for their degrees of expression on variations in external conditions. Changes of temperature or diet will alter this expression and sometimes entirely inhibit it. For example, there is a gene change known in the fruit-fly *Drosophila* which prevents the development of antennae under normal conditions of growth. But when the grubs are amply supplied with vitamin B_2 the 'antennaless' flies become indistinguishable from the normal wild type [4]. Thus evidently the genetic difference concerned in this case depends on ability or inability to do something that is done by the molecule of vitamin B_2. We have equated the action of a specific gene with that of a specific enzyme. Although it is going to be more expensive to test the influence of nutrition on the expression of hereditary differences in man, we can hardly doubt that diet will prove as effective in man as in the fly.

Thus from both ends we see the machinery of heredity being pulled to pieces. It is chemical machinery, but the molecules that are concerned are enormously varied in shape and size. Some of the systems they work are most easily studied in the breeding-bottle, others in the test-tube, and others again under the ultra-violet or electron microscope. Gradually by these means we shall discover how they all work together. And, when we do, we shall find that while the old distinction between the living and the non-living is clear enough, the distinction between chemistry and biology will have become merely one of technique.

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Some eighteenth-century chemical societies

JAMES KENDALL

In the eighteenth century, chemistry was a fashionable pursuit in Britain, and was cultivated at least as much by the inquiring amateur as by the professional scientist. It is therefore not surprising that at this period chemical societies began to take shape. Professor Kendall tells the story of some of these early societies, including the University of Edinburgh Chemical Society, which he shows to have been in existence as long ago as 1785.

The Chemical Society of London planned to celebrate the hundredth anniversary of its foundation in 1941, since its official records state that 'on the 23rd of February, 1841, twenty-five gentlemen interested in the prosecution of Chemistry met together at the Society of Arts to consider whether it be expedient to form a Chemical Society.' Formal celebration of this centenary has been, of course, postponed owing to the war, but in view of the impression that is still prevalent that the Chemical Society of London was 'the first chemical society in the world,' it appears opportune now to present, in brief, the information available regarding a number of other chemical societies which were in existence even before the conclusion of the eighteenth century.

James Woodhouse.

In very olden days, chemists did not forgather merely as chemists; they merged themselves in broader organizations such as the Royal Society. The 'chemical revolution' which had its real beginning with the work of JOSEPH BLACK and which culminated in the overthrow of the phlogiston theory by LAVOISIER aroused, for the first time, a popular interest in the special science of chemistry. Until recently, world priority among the chemical societies that resulted therefrom was by general agreement conceded to the Chemical Society of Philadelphia, founded by JAMES WOODHOUSE in 1792. The distinguished chemical historian EDGAR F. SMITH [7], late Provost of the University of Pennsylvania, may be quoted in this connection:

> This was the first chemical society in the world. As far as can be learned, Woodhouse was its first and only president. This society lived about seventeen years. Its members favoured Lavoisier's doctrine of combustion. The minutes of the society have never been found, although diligent search has been made for them.

Copies of a number of publications of the society, however, have been preserved, and reproductions of the title-pages of two of them are shown on p. 107. The oration of THOMAS P. SMITH was purely historical and did not contain any new experiments, but ROBERT HARE's memoir on his invention of the oxy-hydrogen blowpipe represents a real landmark in scientific discovery.

The title of the Chemical Society of Philadelphia was not questioned until 1935. In April of that year, the Edinburgh University Chemical Society met to celebrate its Diamond Jubilee, being under the impression that it was founded only sixty years previously, and I was requested to prepare a speech for the occasion. Reading SIR WILLIAM RAMSAY's biography of Joseph Black to obtain some historical material for this oration, I came across the statement [6] that, among the correspondence of Joseph Black, Ramsay had discovered a sheet of paper, of which only the date, 1785, was in Black's handwriting, entitled 'List of the Members of the Chemical Society.' Ramsay remarked regarding this as follows:

> This may have been a society of persons residing in Edinburgh interested in Chemistry, but is more

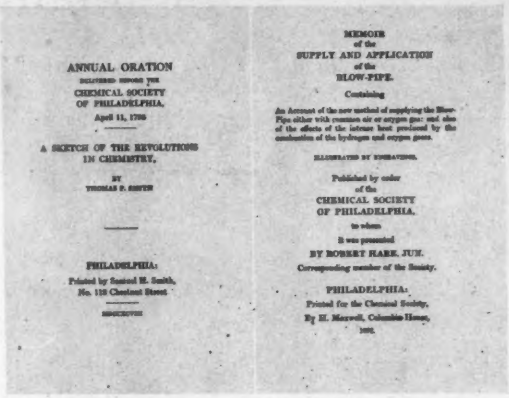
likely to have been a general society. . . . The only name that I can recognize is that of Dr Thos. Beddoes [the founder of the Pneumatic Institute and the 'discoverer' of Sir Humphry Davy]; the names themselves would indicate that their possessors belonged to all parts of the kingdom.

The complete list of names—fifty-nine in all—is reproduced below:

John Webster	Hen. N. Ward	J. Alderson
Wm. Scott	Morgan Deasy	J. McElwaine
— Halliday	H. Pache	T. Gill
Jas. Forster	Jno. Gay	T. Willson
Sam. Black	Tho. McMorran	Frs. Montgomery
Jno. Black	Adam Gillespy	Thos. Swainson
Jas. Plumbe	Thos. Burnside	Archd. Webb
Wm. Johnston	Corn. Pyne	J. Crumbie
Thos. Clothier	J. Unthank	Geo. Marjoribanks
Henry Johnston	J. Barrow	T. Grieg
Peter Gernon	J. Donavan	J. Parr
Robt. Ross	Saml. Macoy	Alex. Stevens
L. van Meurs	G. Tower	Wm. Symonds
(amteemann batavis)	J. Sedgwick	Thos. Beddoes
Hugh Brown	T. Skeete	J. Thompson
John Boyton	Wm. Robertson	G. Kirkaldie
Edw. Fairclough	J. Sprole	J. Carmichel
Bicker McDonald	Thos. Cooke	Nich. Elcock
F. Galley	Thos. Edgar	Richd. Gray
An. Mann	Guyton Jolly	J. Hayle

The idea struck me that an examination of the register of students at the University of Edinburgh at that period might identify more of the names in the above list. This register was accordingly consulted, and within a quarter of an hour it was established that no fewer than fifty-three out of the fifty-nine were students attending Black's class in chemistry at Edinburgh University during the years 1783–87. Thanks to the kindly zeal of DR ALEXANDER MORGAN, five of the missing six were also subsequently traced as registered students of Joseph Black between 1780 and 1788. The only name on the list definitely unlocated is that of Peter Gernon.

In the light of the above discoveries, it became my pleasant duty to inform my fellow-members of the Edinburgh University Chemical Society at their 'Diamond Jubilee luncheon' that they had been called together under false pretences, since they were actually celebrating their Sesquicentenary! For it is quite plain that the society of 1785 was not, as Ramsay surmised, a *general* society. It was, on the contrary, a society consisting of those members of Black's class with a special interest in chemistry—in other words, it was the Chemical Society of the University of Edinburgh. How long it survived after 1785, or how long it existed prior to 1785, we have at present no knowledge, but now that the origin of its membership has been fixed the possibility, noted by Ramsay, of locating 'some one of their descendants in possession of some record of its



ANNUAL ORATION
DELIVERED BEFORE THE
CHEMICAL SOCIETY
OF PHILADELPHIA,
April 15, 1799

A SKETCH OF THE REVOLUTIONS
IN CHEMISTRY,
BY
THOMAS P. SMITH

PHILADELPHIA:
Printed by Samuel H. Smith,
No. 118 Chestnut Street

MEMOIR
of the
SUPPLY AND APPLICATION
of the
BLOW-PIPE.
Containing
An Account of the new method of supplying the Blow-Pipe either with common air or oxygen gas: and also of the effects of the intense heat produced by the combustion of the hydrogen and oxygen gases.
ILLUSTRATED BY ENGRAVINGS.
Published by order
of the
CHEMICAL SOCIETY
OF PHILADELPHIA,
to whom
It was presented
BY ROBERT HARE, JUN.
Corresponding member of the Society.
PHILADELPHIA:
Printed for the Chemical Society,
By H. Maxwell, Columbia House,
1802.

proceedings and history,' is clearly much more likely of realization.

Nineteen out of the fifty-nine members are on the list of medical graduates of the University of Edinburgh between the years 1784–90. This list also gives the nationality in each case, and it is interesting to find that, of the nineteen, only three were native Scots, three English, and the residual thirteen all Irish! Joseph Black was himself, of course, of Belfast ancestry, and the proportion of Irish students in the Scottish universities has always been significant; but such a preponderance as this is very surprising. Whether its Irish element was responsible for the temporary disruption of the society (it is ominous that Bicker McDonald and J. Unthank were both Hibernians) is a question that, perhaps just as well, we are not in a position to press.

There were, however, at least three other chemical societies existent in Scotland prior to 1801 [1], [2]. The first of these flourished in the University of Glasgow as early as 1786; among its members were JOHN MACLEAN, CHARLES MACINTOSH and JOHN THOMSON. John Maclean later became the first Professor of Chemistry in the College of New Jersey (now Princeton University), and it is stated in his biography [4] that:

> at the University he was, while yet a lad, a member of the Chemical Society, a club which appears to have met at the University, with the permission of the College authorities, if not under the oversight of the Professors. The members submitted, for the consideration of the Society, papers and essays upon various matters connected with the object of their association, and some of these papers seem to have foreshadowed the eminence which the authors of them attained in after life, as proficients in the art of Chemistry.

One of seven papers which Maclean himself read before the society, dated 29th March [1786?], contains a reference to DR WILLIAM IRVINE, Lecturer in Chemistry at Glasgow University. Irvine died in the summer of 1787, and on 18th October of that year DR A. EASON of Manchester remarks in a letter [3] to Charles Macintosh (the inventor of the waterproof coat):

'How does your chemical society get on? I am afraid, badly, since poor Irvine is gone. However, you must keep it up.'

It was presumably this same society to which reference is made in the biographical notice of Dr John Thomson, Professor of Medicine in the University of Edinburgh, by his son Dr William Thomson [8]:

> At the beginning of the winter session of 1788–89, Mr John Thomson went to Glasgow to attend the medical classes. Besides prosecuting the study of anatomy with ardour, he attended the lectures of Dr Cleghorn, who was lecturer on chemistry in the college, an office which had been successively held by Cullen, Black, and Irvine. He also joined a chemical society, which contained several members who afterwards attained great eminence as practical chemists. The doctrines of Lavoisier had just been made known, and gave much interest to the proceedings of young and ardent cultivators of chemical science, among whom it may be supposed that they found a readier reception than among those who, before adopting the new doctrines, had previously to unlearn the old.

A second chemical society, however, was founded in Glasgow in 1798; its president in 1800 was WILLIAM RAMSAY, grandfather of Sir William Ramsay. The minute book of this society for the period 8th October, 1800, to 25th March, 1801, is now in the possession of the Royal Philosophical Society of Glasgow [10]. It consists almost entirely of a record of experimental work by the society, apparently carried out at its meetings, which were held generally more frequently than once a month.

Simultaneously we find Dr John Thomson [9] in Edinburgh converting a Natural History Society, probably at the Royal College of Surgeons, into a Chemical Society, of which Lord Brougham and Lord Lauderdale were members. In a letter to his friend Mr Allen, dated 12th June, 1800, he wrote:

> Lord Lauderdale and I made the galvanic experiment last week, and I exhibited it to the Society on Saturday. We are getting tubes with gold wires and glass stoppers to try its effects on caustic liquids, and we are getting a very broad plate of zinc made, to try whether the increase in power be in proportion to the increase of surface. In that case his Lordship's whole service of plate will be converted into a galvanic battery!

There were, thus, before the end of the eighteenth century, no fewer than four chemical societies instituted in Scotland—a truly admirable manifestation of the clan spirit. It is, furthermore, not unreasonable to regard the Chemical Society of Philadelphia as a daughter society of that at Edinburgh in 1785. The medical school of the College of Philadelphia (now the University of Pennsylvania) was instituted in 1765 under strong Edinburgh auspices, and the coat of arms of the University of Edinburgh is still to be seen above the entrance to one of its original buildings. JOHN MORGAN, who first taught chemistry there, and BENJAMIN RUSH, who succeeded him in 1769 as the first full-time Professor of Chemistry in America, were both students of Joseph Black in Edinburgh. With such an intimate connection between the two centres, the existence of a chemical society at Edinburgh University, sponsored by Black, would certainly be a matter of common knowledge in the College of Philadelphia, and when James Woodhouse (then a young man of 22) founded the Chemical Society of Philadelphia in 1792 he may quite plausibly be pictured as following, consciously and deliberately, in the footsteps of Joseph Black.

In 1937, after noting this galaxy of eighteenth-century chemical societies in Scotland [2], I ventured to conclude with the provocative statement that it would be interesting to ascertain when the custom first spread into the degenerate South. This challenge was answered two years later by PROFESSOR J. C. PHILIP, who informed me that a chemical society met in London as early as 1782. The only direct reference to this society is in the Journal of JOHN PLAYFAIR, Professor of Natural Philosophy in the University of Edinburgh [5]:

> 'Chemistry is the *rage* in London at present. I was introduced by Mr B. Vaughan (with whom I became acquainted in Edinburgh while he studied at the University there) to a chemical society, which meets once a fortnight at the Chapter Coffee-house. Here I met Mr Whithurst, Dr Keir, Dr. Crawfurd, and several others.'

Playfair goes on to record how he also saw DR PRIESTLEY, 'who has made so great a figure in the world.' Priestley was then 'particularly engaged in some experiments to prove that inflammable air is the same thing with phlogiston,' but Playfair was too canny a Scot to be convinced.

Are we to regard this Chemical Society of London, existent in 1782, as displacing the Edinburgh University Chemical Society, existent in 1785, from its title of 'the first chemical society in the world'? Personally, I do not think so. It will be noted that the London society to which the Edinburgh professor was introduced had a suspiciously Caledonian flavouring—Mr B. Vaughan was certainly one of Black's students, and two of the other three members named by Playfair are obvious Scots. Is it not likely that this also constituted an offshoot—the 'London branch'—of Joseph Black's original society, the exact date of the founding of which is unknown?

Joseph Black. *G. Bell & Sons*

In any case, the wealth of material that has already come to light encourages the hope that further research will reveal the existence of still more chemical societies of the Black-Priestley-Lavoisier era. It appears probable that one such society flourished in Manchester before 1787, since Dr Eason's letter to Charles Macintosh of that date, already quoted, contains the sentence: 'We intend another volume of our transactions by next spring.' If this article inspires examination of local records of the period leading to additional discoveries, its purpose will have been achieved. Meanwhile, congratulations may be extended to the present Chemical Society of London as the first chemical society in the world to complete a hundred years of continuous existence. May the triumphant celebration of its centenary be witnessed in the very near future!

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Plastics and their application

SIR EDWARD APPLETON

No synthetic substances find wider or more diverse applications than plastics, and their usefulness continues to increase. Sir Edward Appleton discusses the structure and properties of some of the principal types, and his illustrations reveal their adaptability for surprisingly various purposes. Electrical apparatus, brushes, gun-turrets, boats, and even gear wheels —these are a few of the articles made wholly or partially of plastic materials.

FIGURE 1 – *Test extrusion of soft polyvinyl chloride sheathing.*

War-time lends a special urgency to the task of reducing the number of operations in manufacture. Some manufactured articles are of intricate shape and, to produce them from solid materials, much cutting, turning, drilling, and grinding may be needed. It is for such articles as these that plastics, if materially suitable, can be used to best advantage, for, essentially, their shape is then determined by a single operation.

The plastics industry, which has arisen only in relatively recent years, depends on the use of organic materials which, usually by the application of heat, can be rendered plastic and thus formed to a desired shape, which is retained when the plasticizing agency is withdrawn. The materials seldom occur naturally, and generally are entirely synthetic. As examples one might refer to the resins made by the interaction of phenol (carbolic acid) and formaldehyde or of urea and formaldehyde. Another group of substances is made by polymerization, i.e. by the union of small molecules of liquids, or even gases, to form large molecules representing plastic solids. Of such origin and type are polystyrene and polyvinyl chloride. Other plastics, such as cellulose nitrate and cellulose acetate, made by the action of nitric or acetic acid on cellulose, are derivatives of naturally occurring organic materials.

'Plasticity' is generally associated with substances of high molecular weight. These macromolecules may consist either of long chains or of mesh-like structures. The chemist can now synthesize macromolecules (or modify naturally occurring macromolecules) to give products possessing chemical and physical properties which to some extent can be predicted. He is rapidly becoming expert, as someone has aptly put it, at 'tailoring the molecule.' He does all this using only a few basic raw materials: coal, petroleum and cellulose.

It has been found, for example, that plastic substances of non-polar or hydrocarbon character are excellent high-frequency dielectrics. Synthetic resins consisting of macromolecules derived

FIGURE 2 – *Injection-moulded polystyrene: used in high-frequency coil formers.*

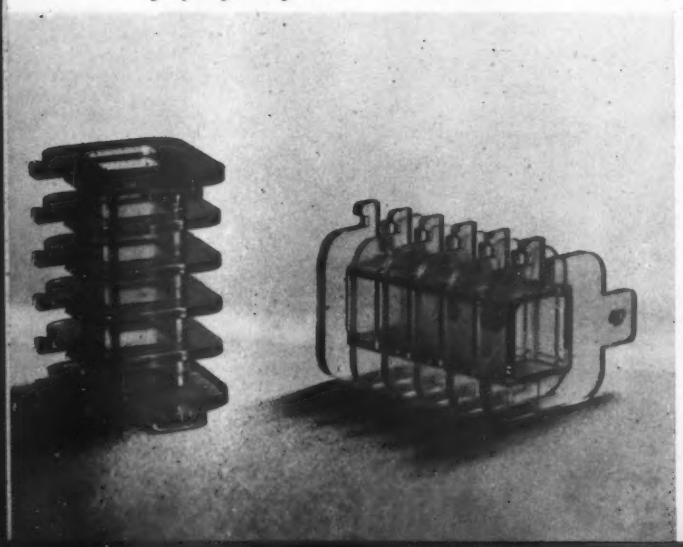


FIGURE 3 – *Ducts of cellulose acetate used in aircraft.*

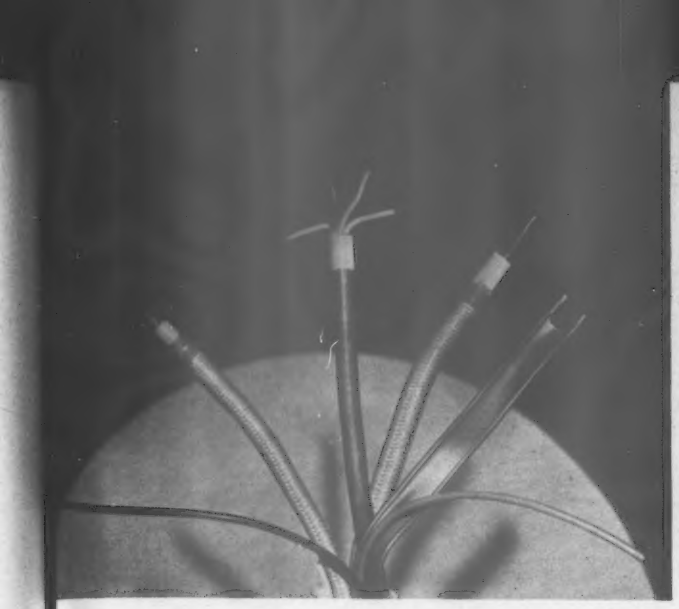


FIGURE 4 – *Electric cables insulated with extruded polyvinyl chloride.*

FIGURE 5 – *Boat moulded from resin-bonded plywood in course of manufacture.*

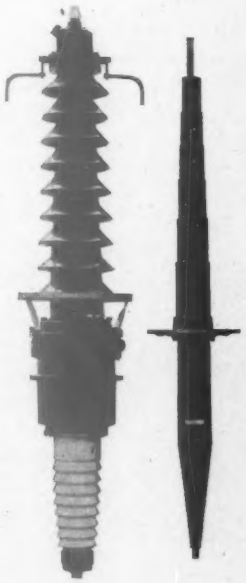
from hydrocarbons such as styrene, isobutylene, and ethylene combine the desirable dielectric properties with fair mechanical strength. Another interesting and still more recent development has been the synthesis of resins which, when in a plastic condition, can be drawn into valuable fibres for textile uses or into filaments for use as bristles, gut, etc. Natural fibres consist of cellulose or protein macromolecules oriented in the direction of the fibre axis (see this Journal, Vol. I, No. 2, pp. 70–73). The chains of synthetic linear macromolecules are generally arranged in random fashion, and only those plastics the molecules of which can be similarly oriented by stretching while in the plastic state have proved suitable for the production of fibres. Notable successful examples are nylon, which is an idealized protein, and vinyon, which possesses excellent chemical resistance. In a similar manner, many macromolecules have been synthesized which have rubber-like properties.

The development of glass-clear synthetic resins has been largely empirical, but the value of the products, such as polymerized methylmethacrylate, is now well established. Transparency, toughness, and ease of working ensure a permanent future for this type of material.

The macromolecules hitherto used as industrial plastics have a 'backbone' of linked carbon atoms, but resins (polymerized methyl silicones) have recently been developed in which the 'backbone' consists of silicon and oxygen atoms. These have been suggested for use as electrical insulation at high temperatures, since their resistance to heat is greater than that of the carbon-linked polymers[1].

While the shaping of plastics into useful articles usually depends basically on the application of heat, the exact technique followed may vary considerably in different cases, and is influenced by the nature of the resin, the character of the article to be fabricated, and the presence and nature of any reinforcing or filling ingredients with which the resin may be compounded.

FIGURE 6 – 132 *kV. oil circuit-breaker bushing, showing alongside the resin-insulated condenser bushing without the porcelain and current transformer housing.*



The simplest way of moulding plastics is by shaping sheets of material, while softened by heat, over wooden forms. Cellulose acetate and polymethylmethacrylate are fabricated into cockpit covers, windows, etc., for aircraft by this process. A method particularly suited to producing rods, tubes and similar simple shapes in continuous lengths is to extrude the heated plastic by a worm through a die. An example of this process, growing in importance, is the production of sheathing from

[1]For further information on these materials, see Rochow and Gilliam, *J. Amer. Chem. Soc.*, 1941, **63**, 798; Brit. Pat. No. 542655, 21st January, 1942.

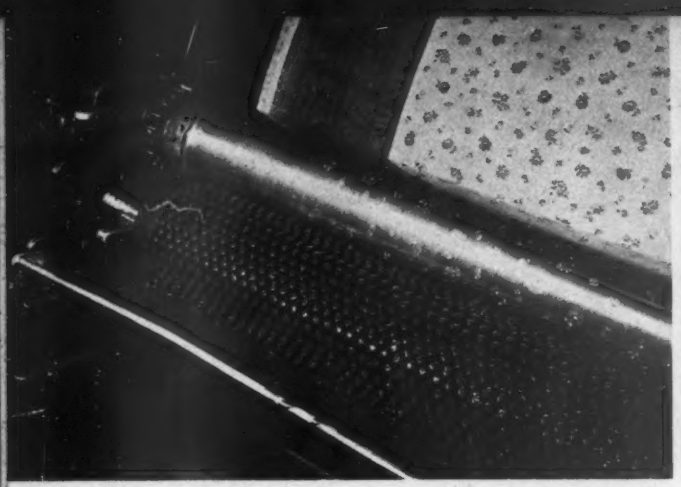


FIGURE 7 – *Nylon-bristled brush for furnishing colour to a printing roll.*

FIGURE 8 – *Resin-impregnated paper strips being wound in spiral fashion on to a conductor for insulation.*

plasticized polyvinyl chloride for use in insulating electric cables.

A major development of the plastics industry has been the compression moulding process, in which a moulding powder, compounded from wood-flour, wood-pulp, cotton-flock, chopped fabric, etc., and a synthetic resin, is heated, under considerable pressure, in an appropriate mould. Another method of fabrication is the injection-moulding process, in which material in the plastic state is forced through a heated die into a chilled mould. Cellulose acetate, polystyrene, etc., are often shaped in this way, the process being capable of rapid output, as three to four complete cycles a minute can be performed.

The mechanical strength of synthetic resins themselves, even when compounded with materials such as those already mentioned, although adequate for many applications, is not as high as theoretical considerations indicate to be possible. From such considerations alone, plastics should be very strong, but, in practice, they are relatively weak. Now, the tensile strength of unfilled plastic material can be calculated theoretically on the assumption that, in rupture, either (*a*) the exchange forces between neighbouring atoms are overcome, or (*b*) the breaking stress is such that the long molecules are drawn apart in spite of the VAN DER WAALS' forces expressing the electrostatic attraction between them. In the case of the familiar phenol - formaldehyde, the ratio of the theoretical tensile strength to the practical value is found to be 500 on assumption (*a*) and 5 on assumption (*b*).

Much, of course, may be done by suitable reinforcement. Mineral reinforcements, such as asbestos fibres, are valuable as conferring resistance to heat and chemical attack, while abrasive metallic powders, slate dust, etc., may be useful to satisfy special requirements. To get a substantial degree of increased mechanical strength, however, strong fibrous reinforcements are needed. Such reinforcements are usually in the form of

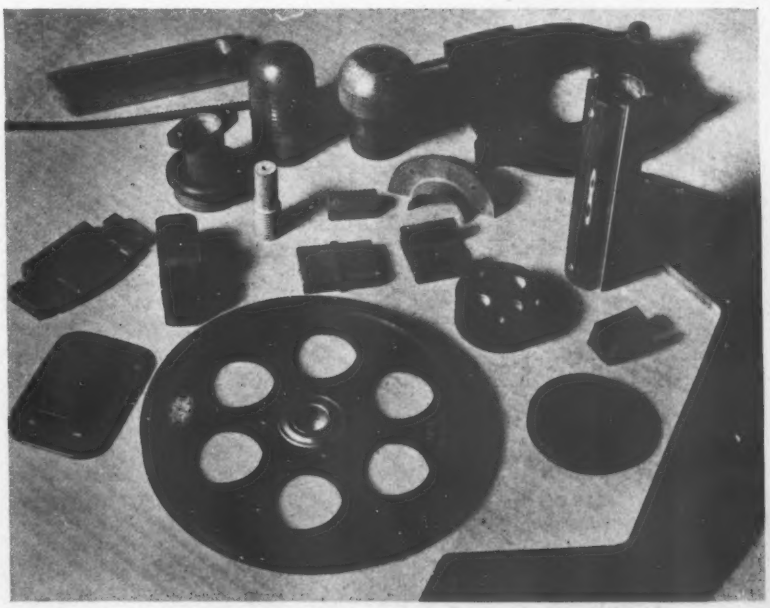


FIGURE 9 – *Fabric-reinforced moulded components used in aircraft.*

FIGURE 10

FIGURE 11

FIGURE 12

paper or fabric, the layers of which, impregnated with the resins in solution, are bonded together under heat and pressure. The resulting laminated sheet can be shaped to a certain extent, and is particularly useful as stock material from which bearings and silent gear wheels can be made. Impregnated paper may also be wound on to a heated mandrel to give tubes used for electrical purposes, such as transformer bushings.

Finally, plastics are now being used on an increasing scale in the manufacture of moulded plywood. The veneers are bonded with synthetic resin glues by a process which is a development of normal plywood and plastic moulding techniques. The advantages of using these synthetic cements are that the laminated products are strong and waterproof, and that parting of the plies does not occur in damp conditions.

FIGURE 10 – *Gear wheels machined from fabric-base laminated sheet.*

FIGURE 11 – *Air extractor housing and impeller moulded from filled phenolic resin and resistant to corrosive fumes.*

FIGURE 12 – *Reaction vessel made from asbestos-reinforced phenol-formaldehyde and possessing great resistance to chemical attack.*

The photographs in this article are reproduced by the courtesy of the following firms: Bakelite Ltd., BX Plastics Ltd., Distillers Co., Kestner Evaporator and Engineering Co., Micanite and Insulators Co., Plastics and Tenaplas Ltd.

FIGURE 13 – *Gun-turret made from thermoplastic polymethylmethacrylate.*

Disease-resistant plants

F. T. BROOKS

Many valuable crop plants are liable to serious diseases. Fighting these diseases by chemical methods is generally either impossible or too expensive. Botanists and plant breeders have therefore adopted an alternative course, and by systematic hybridization have produced, of many important plants, varieties which are highly resistant to disease. Notable results have been attained with wheat, potatoes and tomatoes.

Disease takes as heavy a toll of cultivated plants as it does of human beings. Chemists have played a prominent part in controlling plant diseases, even though, as yet, chemotherapy in plants has no striking successes to its credit as in the cure of certain human maladies. The lifeless sap of plants and its movements in the tissues are quite unlike the living blood-stream of animals; consequently, the possibility of applying the methods of chemotherapy successfully in plants is still remote, although some slight progress has been made by injecting diseased woody tissues in trees with substances toxic to the invading fungus but harmless to the plant. In the domain of plant pathology the outstanding successes of chemists concern the prevention of foliage and fruit diseases by spraying or dusting the plants with fungicides, and the elimination of seed-borne diseases by dusting the seed with fungicidal substances, especially organic mercury compounds. There are, however, large groups of plant diseases which cannot at present be controlled by chemical means, either through inherent difficulty or owing to excessive cost. Many diseases caused by rust fungi are in this category and so are several diseases contracted through the soil. In North America, wheat rust has been experimentally controlled by frequent dustings with sulphur from low-flying aeroplanes, but the cost is excessive. Similarly, although disease germs in the soil of a glasshouse can be destroyed by heat or chemical means, there is no known method of eliminating parasitic soil fungi over large areas of soil without extravagant cost or rendering the soil unsuitable for plant growth.

Fortunately, Nature herself provides the means in many instances of controlling or appreciably alleviating these difficult plant diseases. Practically all crop plants which have been in cultivation for long ages exist in the form of innumerable varieties which differ remarkably in their reaction to specific diseases, some being very susceptible while others are resistant or even immune to attack. It may be asked why varieties susceptible to disease continue to be grown. The reason is that many susceptible varieties give a heavy yield of high-quality produce, especially in seasons when disease is not unduly prevalent, while many resistant varieties crop poorly or suffer from some other serious commercial defect. It is obvious that if, by hybridization, resistance to disease could be combined with the valuable attributes of the susceptible variety, definite progress would be made. Some of the earlier plant hybridists had this in mind towards the beginning of the nineteenth century—for example T. A. KNIGHT in Britain—but little advance was made because at that time there was no clue to the mode of transmission of hereditary characters in plants and animals. Another notable pioneer in this respect was WILLIAM J. FARRER, who from 1886 onwards deliberately set about the breeding of wheats in Australia to resist rust attack. At that time rust laid a heavy toll on the yield of Australian wheat year after year. Farrer achieved much success even before 1900, which, as will be seen, was a critical year in the history of plant genetics. The varieties of wheat now grown in Australia are chiefly derivatives of those which Farrer produced, and they are much more resistant to rust than those grown before he began his work. Between 1890 and 1920 wheat production in Australia increased from 27 million to 144 million bushels, and this was largely due to the introduction of varieties created by Farrer.

In 1900 an event happened which has had a profound and even revolutionary influence on plant-breeding methods ever since. In that year was rediscovered a most important paper on the laws of heredity in plants by GREGOR MENDEL, abbot of the monastery at Brünn, Czechoslovakia,

which had been published in an obscure periodical in 1866. Three European botanists independently called attention to the vital importance of Mendel's paper and announced that they had confirmed Mendel's results. How such a paper came to be overlooked for so long is a mystery, but even CHARLES DARWIN, who died in 1882, was unaware of Mendel's discovery. Mendel experimented with different races of garden peas (*Pisum sativum*) and showed that such characters as stature of plant, colour and shape of seeds, and colour of flowers were transmitted according to definite laws in the progeny of the hybrids established between races differing in such characters. Furthermore, it was clear that hybrids established between races differing in two characters gave some progeny showing different combinations of characters from those in the original parents. Mendel's discovery is the greatest ever known in plant breeding, and investigators in different countries soon showed it to be of general application. Here, then, at last was a clue which would enable plant breeders deliberately to synthesize new varieties of crop plants. Plant breeding was no longer a hazardous art; to a considerable extent it had become an exact science. To return to wheat: it was now possible to envisage the creation of new varieties which, while retaining the valuable commercial qualities of the old varieties, would also be resistant to such diseases as rust.

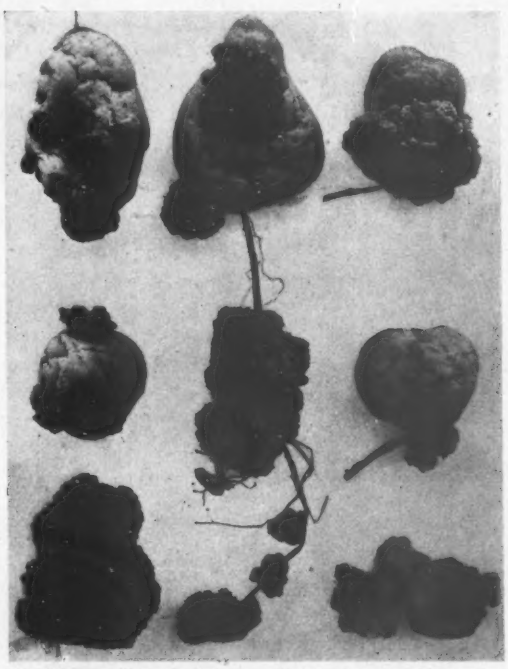
Sir Rowland Biffen.
From the painting by Kenneth Green.

In 1899 R. H. BIFFEN (now SIR ROWLAND BIFFEN) was appointed botanist to the newly founded Department of Agriculture in Cambridge University, and in this post he set himself the task of trying to improve the productivity and quality of English wheat. With the rediscovery of Mendel's paper in 1900 he was provided with a potent instrument for the prosecution of his investigations. One of the first matters to engage his attention was an endeavour to breed wheats less susceptible to yellow rust (caused by the fungus *Puccinia glumarum*) than those commonly cultivated at the time. In England, yellow rust is the most serious rust of wheat, but in certain other countries stem rust (*Puccinia graminis*) is more important. It was not then known whether susceptibility and resistance to yellow rust were transmitted hereditarily in accordance with Mendel's law. Biffen therefore crossed a very resistant wheat (American Club) with a very susceptible one (Michigan Bronze), and showed that when the hybrid was self-pollinated segregation of these characters occurred in the next generation in accordance with Mendelian expectation. The full results were published in the *Journal of Agricultural Science* in 1907. Thus for the first time it was demonstrated that susceptibility and resistance to a specific disease are characters which are transmitted hereditarily in a perfectly definite manner, like certain other plant characters. The way was now open for plant breeders throughout the world to attempt hopefully to create new varieties of crop plants resistant to certain parasitic diseases which were difficult or impossible to control by the usual means. Biffen applied the information he had newly acquired to build up a variety of wheat which would retain the valuable qualities of the old varieties and be at the same time resistant to yellow rust. He crossed together Square Head's Master—a popular heavy-cropping variety but susceptible to yellow rust—with an exotic variety, Ghurka, which though cropping poorly in England was very resistant to this rust. Some of the segregates from this process of hybridization were found to possess in greater or less degree the valuable qualities of Square Head's Master together with resistance to yellow rust. These new types were tested for some years, and the best one, Little Joss, was put on the market and is now one of the most extensively grown wheats in this country. Because of its resistance to yellow rust it crops even more heavily than Square Head's Master. In the great wheat-producing countries of the United States, Canada, Australia, and India, stem rust (*Puccinia graminis*) is the chief menace to production. Departments of Agriculture and state-aided institutions have devoted much energy during the last forty years to the creation of wheats resistant to this rust and otherwise suitable to local conditions. Various complications have arisen, notably because this

fungus exists in the form of many physiologically distinct races which differ in their incidence from year to year. It is useless, therefore, to breed a wheat resistant to only one of these races: what is required is a variety resistant to all the common races liable to occur in a particular area. In the great wheat belt of North America two varieties have been produced in recent years which fulfil this requirement, viz. Thatcher, made at the University of Minnesota, and Renown, created by the Canadian Department of Agriculture at Winnipeg. These varieties are tending to replace the well-known Marquis wheat because of their greater resistance to rust. In Australia varieties are now available even more rust-resistant than those produced by Farrer.

The problem of making disease-resistant crop plants is one which every important agricultural country must face. Each country must work out its own salvation. To be commercially successful each new variety must be adapted to local conditions, and, as already pointed out, the deleterious fungi or their races may differ from country to country. This is now universally recognized and the agricultural authorities of all countries are taking steps to produce varieties suitable to their own countries. Plant breeders, and plant pathologists in association with them, have a full programme for many years to come. In many instances it is important to produce varieties resistant to more than one disease, and such syntheses are necessarily slow. A variety bred to resist one disease may be very susceptible to another, so that only gradually can crop plants be built up which are resistant to several serious diseases.

Potatoes are a crop afflicted by a number of important diseases, not one of which can be overlooked by the plant breeder seeking improved varieties. To mention the most important troubles: wart disease (*Synchytrium endobioticum*), contracted from the soil, transforms the tubers into inedible monstrous growths (*see below*); blight (*Phytophthora infestans*) destroys the haulm, reduces the crop and rots the tubers; and viruses may so impede growth as to render the crop negligible. Admittedly, blight can be controlled by spraying the haulm with copper fungicides, but the plant breeder visualizes the eventual production of varieties immune to wart, resistant to blight, and uninjured by viruses. Inspectors of the English Ministry of Agriculture were the first to discover that some varieties are immune to wart, and in recent years new varieties have invariably been tested for their reaction to this disease before being grown commercially. The varieties of potatoes commonly grown in Britain at present are all more or less susceptible to blight, and progress towards the achievement of resistant types is slow, partly because of the extremely hybrid nature of present domestic stocks. SALAMAN, formerly of the Potato Virus Research Station, Cambridge, and REDDICK, in the United States, have, however, made some advance in this direction by hybridizing certain varieties with a Mexican species of *Solanum* which is immune to blight. In South America—the home of our domestic potato (*Solanum tuberosum*)—and in Mexico there are many varieties of potato not in European cultivation, and several closely related wild species of *Solanum;* these constitute a great reservoir of genetical material for use by plant breeders in the creation of new varieties. In recent years the U.S.S.R., the U.S.A., Sweden, Germany, and the Imperial Agricultural Bureaux of the British Empire have sent expeditions to Mexico and South America to collect this valuable material. The British expedition returned in 1939, and the collections are now being investigated by the Imperial Bureau of Plant Genetics in association with the Plant Breeding Institute at Cambridge. Perhaps with the new material now available the perfect potato will be produced: free from disease, of good quality and



Wart disease (Synchytrium endobioticum) *of the potato.*

Upper part of silvered Victoria plum tree, one branch of which is dead and bears fructifications of Stereum purpureum.

cropping capacity, and uninjured by moderate frost.

There is hardly a herbaceous crop plant grown in temperate countries which has not been improved in recent years as regards disease-resistance, but space permits mention of only one more example. The interests of growers of crops under glass, e.g. tomatoes, are also being watched by plant breeders. Here leaf mould (*Cladosporium fulvum*) is one of the chief culprits. Canadian workers have hybridized the tomato with the small currant tomato which is immune to attack, and have produced the variety Vetomold, which is both immune and highly productive. Preliminary trials with Vetomold in this country have been very successful.

The production of disease-resistant types of arborescent plants is inevitably slow, and is a formidable undertaking even for institutions which have facilities for experimenting over long periods of years. How valuable it would be in this country if we had a variety of plum with all the good qualities of the variety Victoria and at the same time resistant to silver-leaf disease caused by the fungus *Stereum purpureum!* This fungus invades the woody tissues of the tree through wounds and speedily causes death, fructifying on the dead branches (*column* 1). Attention to plant hygiene minimizes the risk of invasion, but a similar variety resistant to this disease is greatly needed by fruit-growers.

With tropical crops much attention has been and is being paid to the breeding of resistant types. Losses from epidemic disease are likely to be particularly severe under tropical conditions. One of the most notable achievements in the tropics is the production by the Dutch in Java of varieties of sugar-cane uninjured by certain virus diseases, by means of which the output of sugar has been greatly increased. The banana industry in Jamaica and certain parts of Central America is now threatened by Panama disease, caused by a fungus contracted from the soil. There is no known means of control apart from the breeding of a resistant variety. The tropics of the Old World have been ransacked for banana varieties in the hope that some of them would prove resistant to the disease. These were first sent to the Royal Botanic Gardens, Kew, and kept in quarantine there to ensure that they were not afflicted by other serious diseases before being sent to the West Indies. Some of these varieties have proved to be resistant to Panama disease, and geneticists in Jamaica and Trinidad are now using this material for hybridization. It is not, however, sufficient to produce a banana which fruits well and resists the disease; it must also have the valuable qualities of easy and safe transport by sea over long distances possessed by the present Gros Michel variety.

Another disease which is causing concern in the West Indies and contiguous lands is witches' broom of cacao (cocoa), again caused by a parasitic fungus, and again difficult if not impossible to control by the usual means. A few years ago a British expedition was sent into the upper reaches of the rivers Amazon and Orinoco to collect wild varieties of cacao resistant or immune to this disease. The material so collected is now being utilized by plant breeders in Trinidad.

Even the humble flower gardener, as well as the cultivator of broad acres, wants disease-resistant varieties. For rust-resistant antirrhinums he will probably not have long to wait, since investigations in California and at the Royal Horticultural Society's gardens at Wisley, Surrey, have shown that good sturdy types can be produced.

The propagation of sound in the atmosphere

E. G. RICHARDSON

The transmission of sound in the air shows many peculiarities, frequently of a very surprising kind. Explosions and gunfire are often inaudible in regions comparatively close at hand, while distinctly audible at greater distances. Echoes of a foghorn may sometimes be heard for as long as 15 seconds after the original sound has been cut off. In this article, Dr Richardson provides an interesting account of recent investigations carried out on the subject by British and other workers.

Much work has been done in the last two decades on the transmission of sound to great distances from a powerful source, such as that produced by the firing of a heavy calibre cannon or by the blowing up of dumps of unwanted explosives after the last war. It was observed between 1915 and 1918 that the sound of gunfire from the Western Front was audible in places in the vicinity of London, whereas at intervening places in Kent nothing was heard, even in the presence of a favourable wind gradient. The existence of such 'zones of silence' was confirmed when at prearranged times and places explosions were staged *ad hoc*. In this work, the occurrence of a region where the sound is inaudible in spite of the fact that it is distinctly audible at a greater distance from the source was confirmed. An inner zone of audibility, in which the sound-rays travel directly over the surface of the earth, to be frittered away by expansion of the wave-front and in friction over broken ground, trees, etc., is found to surround the source with an irregular area. Follows the silent zone, in which, although no sound is heard, there are indications of an inaudible pulse of low frequency. Outside this there is the abnormal zone, where the sound reappears with renewed intensity, but apparently taking an exceptionally long time to arrive.

This last factor naturally leads one to suppose that these sound-waves have travelled into the upper regions of the atmosphere and down again, the abnormal intensity on the inner fringe of this zone being ascribed to the convergence of rays which have traversed slightly different paths to this point, and to the absence of friction, other than air damping, in the stratosphere. Since the temperature under normal conditions is known to decrease in the first 17 km. above the earth's surface and, with it, the velocity of sound, we must assume that, in the absence of refraction caused by wind gradients, paths of sound-rays are concave, viewed from above, in these regions. The information on temperature is obtained from pilot balloons —small balloons carrying a cage of instruments to read temperature, pressure, and humidity at the altitude at which the balloon is set to burst, the cage then falling safely to earth under control of a parachute which opens on release from the lift of the balloon. At the present ceiling of pilot balloons, however, there are indications that the temperature is ceasing to fall, and meteorologists postulate a temperature inversion at this height and assume that above this level the stratosphere is so heated by the sun's radiation that warmer regions are rapidly entered. It is evident indeed that something must happen to the sound-waves in this region to turn them back to earth—something, that is, to give a convex track (seen from above) to rays in the stratosphere. Short of a sudden reflection at a barrier formed by a definite discontinuity in atmospheric properties, this implies a region in which the velocity is continually increasing upwards, whereas below in the troposphere the velocity decreases with height.

From the direction at which the sound in the abnormal zone is noted to return to earth, it has been estimated that rays reaching the outer edge of this zone (usually about 200 km. from the source) had an original inclination of 40° to the horizon. It is, then, a matter of putting forward hypotheses for the velocity of sound above 17 km. and testing these against the known time of propagation of the sound from the source within the prescribed surface distance (180 to 300 km.). Such hypotheses must make the summit velocity high, otherwise such rays would not be turned back. The simplest hypothesis seems to be to suppose that above the inversion level the velocity

of sound rises at such a rate that at between 30 and 40 km. the surface velocity is reached again and subsequently exceeded. This gives the ray reaching the outer edge of the abnormal zone a summit level of 70 km. Those with an initial trajectory angle greater than 40° are 'lost,' unless reflected by acoustic clouds. The vertical projections of such sound-rays are shown in figure 1, and the collected results of one such explosion (under the aegis of the International Commission for the Investigation of the Upper Atmosphere) are shown in figure 2, viz. at Kummendorf in December 1925 (after DUCKERT [1]). The zone where the sound was heard at normal velocity is shown in the centre. The abnormal zone of apparently low velocity is indicated by horizontal hachuring. It may be noted that it is more definite to the east of the source in summer and to the west in winter (a general feature on which surface winds have little influence). When one writes 'apparently low velocity' one means, of course, that it is low reckoned in terms of the surface distance. Actually, as we have noted above, it has travelled at abnormally high velocity over the greater part of its trajectory. There are indications, after further silent gaps, of sectors of two more audibility zones (marked in vertical hachures) to the west. These are ascribed to 'ricochets' of the rays at the surface when they come down on their first trajectories, so that the process of penetration to the stratosphere and back is repeated with diminishing intensity. The approximate equality of the lengths of such jumps can be gauged from the separation of the zones on figure 2.

Measurements have also been made in England by WHIPPLE [8], using gunfire as source, with sensitive microphones set up at different stations about 70–100 miles away. These confirmed the seasonal variation noted in the explosion trials; in this series reception was better in the western and north-western directions from the origin (Woolwich or Shoeburyness in the Thames estuary) from May to August, but at the north-eastern station (in Norfolk) in the winter. It is possible that seasonal winds in the upper atmosphere may account for these variations.

We now turn to the hypotheses which have been put forward to explain the track of the sound-rays in the stratosphere, bearing in mind that no hypothesis is tenable which does not give velocities of sound increasing with height.

On the three physical constants appearing in the Laplacian expression for this velocity, pressure

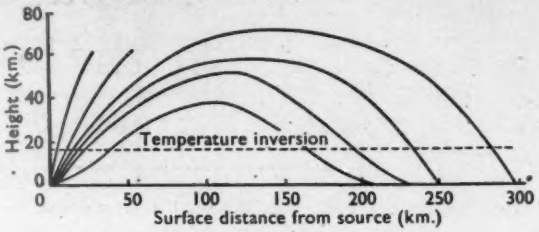


FIGURE 1

per se can have no effect. There remain temperature and composition of the atmosphere as variables. For an increase in velocity, temperature must rise, or the atmosphere must become richer in lighter molecules than it is in the troposphere, or both changes must occur.

Near the surface of the earth, as is well known, the atmosphere consists mainly of the diatomic molecules of oxygen and nitrogen with small admixtures of the rare gases, argon, helium, neon, etc. The latter are monatomic. The question of the number of atoms in the molecule is important, because the ratio of specific heats at constant pressure and at constant volume (which comes into the expression for the velocity of sound) depends on this. For most monatomic

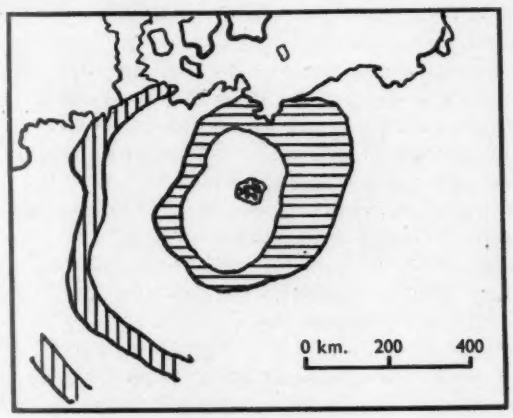


FIGURE 2

gases it is 1·66, for diatomic 1·41, and for triatomic 1·3. Apart from density changes, therefore, the effect of dissociation of the air completely into atoms—if that were probable—would raise the velocity of sound by a mere 8 per cent. It is in fact known that above 25 km. atomic oxygen becomes more and more prevalent, but this condition alone is scarcely likely to produce the increase we are looking for.

Some other information is obtainable from the

spectrum of the aurorae, electrical phenomena known to have their origin in the upper regions of the atmosphere and whose light might be regarded as characteristic of these regions; though this light has, of course, to pass through the troposphere before reaching the spectrometers here. It appears that the helium content of the atmosphere remains constant from the ground up to 20 km., but above that increases slightly relative to oxygen. The existence of hydrogen in the stratosphere has not been confirmed. In any case, we should require a high proportion of this gas to give the required rise in velocity of sound, if the latter is to be ascribed solely to composition. We are therefore led to adopt the rising temperature hypothesis. If, indeed, the effect on velocity is entirely to be ascribed to temperature, we must postulate that, from the inversion at 17 km., the temperature reaches its surface value again at 40 km., and by 50 km. has passed 70° C. Such an idea is quite contrary to the older meteorological theories, and though it is by now generally accepted, little is known of the mechanism by which these layers are warmed. They are, of course, considerably rarefied, so that the sun's radiation is able to reach the gaseous molecules without much absorption by other molecules lying further still on the confines of the stratosphere, whereas the heat which reaches us has been so filtered or reflected by gases and water vapour. This suggestion is rather spoilt by sound-propagation experiments carried out from Russian arctic stations during polar nights. Similar anomalies in the zones were observed to those which persisted in the daytime. It is, of course, possible to retain the solar radiation theory and to postulate that the polar cap stratosphere remained warmed during the night by convection currents or winds from lower latitudes.

Experimental study of atmospheric influences in surface propagation was made in 1870 by TYNDALL for the Trinity House Brethren, who have charge of the navigation lights and sirens round the British coast. The sirens at the South Foreland were chosen for the experiments. He reached the result, surprising at that time, that an overall fog accompanied a favourable perception of the signals. This was not due to the atmospheric moisture itself, but to the fact that fog is an indicator of stable and homogeneous atmospheric conditions. It is when the atmosphere is 'patchy,' i.e. having a diversity of density at different points, with unequal temperature and humidity distribution, that fluctuations occur in the audibility of the sirens, both in time and in space.

Sometimes these patches, in the form of acoustic clouds, caused continuing echoes of the blast lasting as much as 15 seconds after it had been turned off. Owing to the presence of such reflecting patches in the atmosphere a siren giving a continuous note of short duration is sometimes heard better, and sometimes worse, than the crack of a gun giving a short impulse.

MAJOR TUCKER [7] has explored the sound field round the North Goodwin and Casquet sirens. During a typical summer day the intensity of the sound picked up varied irregularly in a 30 to 1 ratio over a period of a few minutes. A favourable temperature gradient for the propagation of sound was experienced when air had passed over a land surface at high temperature and subsequently had its lower strata cooled by passage over the sea in the neighbourhood of the source [6]. In these cases, again, an overall reduction in humidity was generally accompanied by a reduction in audibility.

When the atmosphere is not homogeneous in density at any level the variation is, of course, usually caused by clouds or fog banks. Apart from the grosser type of reflection and refraction caused by obstacles such as these, which are huge compared to the wave-length of all sounds, there is another source of scattering of sound which parallels the same phenomenon in light—that scattering which occurs when light passes through a smoke or other suspension of particles, of the same order of size as the wave-length of the light. Although even the largest raindrops cannot approach the wave-length of bass notes, the lengths of high-frequency sound-waves near the upper limit of the treble are to be reckoned in millimetres. The extent to which obstacles of this kind upset the normal passage of high-frequency or supersonic waves has been exhibited in some recent research [4] in which such a beam has been passed through artificial smoke suspensions of magnesium oxide and lycoperdon spores. (The spores of this fungus are nearly spherical and of uniform size.) The results show that there is a considerable absorption of sound energy as the frequency increases. This is borne out in practice. It is well known that on a misty day, or on one accompanied by rain showers, the 'speckled' character of the atmosphere results in considerable attenuation of high-frequency sounds, while those of lower frequency are left unaffected.

The latter are in fact more likely to be

disturbed in propagation on a gusty day. On such occasions the distorting elements in the sound-field are the eddies set up by turbulence. These can well extend to several feet in diameter and are capable, in spite of their intangibility, of upsetting the propagation of quite long waves, though the actual degradation of energy is not so certain as with solid or liquid obstacles and high-frequency sounds.

Quite recently, EAGLESON [2] has carried out measurements of the absorption of sound in the open air at Bloomington, Indiana, over short distances (200 yards) at audible frequencies, which show well how the 'classical' idea of absorption is set aside when banks of fog, clouds, and rain are about. Whereas theory and practice could be brought to agree within the somewhat surprising figure of 1 per cent. under good homogeneous atmospheric conditions, patchiness of the atmosphere produced vagaries in the readings of the instruments amounting to 10 per cent. of normal after allowing for the effect of average humidity on the anticipated absorption.

There is yet another cause of selective absorption of sound-waves, even in a homogeneous atmosphere. KNUDSEN [3] discovered that the rate of decay of reverberation in a room, after a loud-speaker sound-source had been turned off, varied considerably with humidity. The classical absorption (due to friction and heat-conduction) is quite small in comparison. At a given temperature, the absorption coefficient reaches a maximum at a certain value of the humidity (cf. figure 3). Put another way: at constant humidity, the coefficient of absorption increases markedly with frequency, the effect being more important at large water-vapour pressures. The effect, too, has been pursued into the supersonic range of frequencies [5]. That this is a form of molecular absorption is not in dispute, though the precise way in which a comparatively small number of water molecules can confer rigidity on the oxygen and nitrogen molecules so that they damp the vibrations passed through them is not yet properly understood. At any rate, the experiments add point to the noticeable attenuation of high-frequency waves in Nature, upon which we have already remarked.

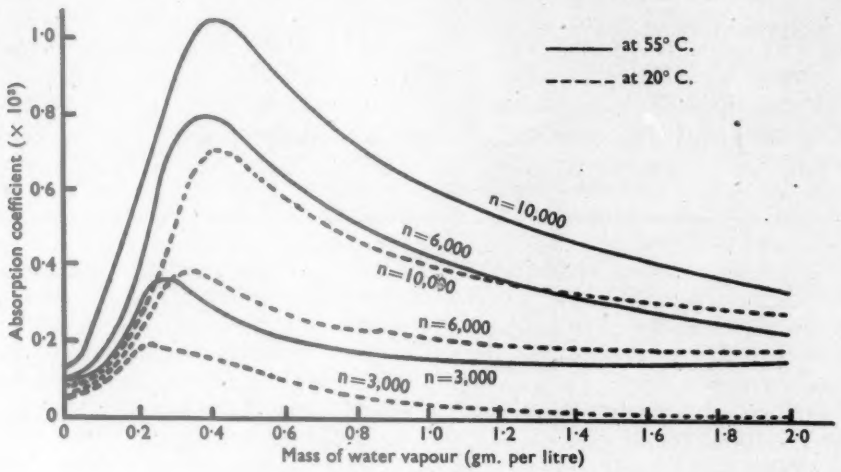


FIGURE 3

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Progress in bacterial chemotherapy

L. P. GARROD

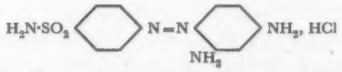
In the short space of seven years, progress in the chemotherapy of microbic infection has effected dramatic changes in medical practice. Pneumonia, cerebro-spinal fever, puerperal fever, and 'blood-poisoning,' which formerly ranked as intractable scourges, are now amenable to treatment. Professor Garrod describes some of the new drugs responsible for this transformation, and offers a convincing explanation of their mode of action.

In countering the attack of microbic infection, a remedy which will destroy the micro-organism itself will clearly be the most certain in its action. If a drug capable of doing this can reach the affected area in the circulating blood, thus pervading it completely, the therapeutic ideal has been attained. It need scarcely be said that most 'antiseptics' are wholly unsuited for such a purpose: they are far more lethal to man himself than to the micro-organisms which attack him. It is broadly true that the more complex an organism, the more readily is it poisoned, and a substance relatively harmless to the human body but nevertheless lethal to a unicellular micro-organism must have exceptional properties and will not be easy to find.

Until recent times a sharp distinction has been drawn in this connection between protozoa and bacteria. The former belong to the animal kingdom, are somewhat more complex in structure and metabolism, and were believed on these grounds to be more susceptible to attack. The efficacy of quinine in malaria and of ipecacuanha in amoebic dysentery has long been practical evidence for this belief. Bacteria, on the other hand, are the most primitive members of the vegetable kingdom. No drug was known which would seriously interfere with their activities within the body, and many microbiologists doubted whether such a substance could exist.

The year 1935 marks the abandonment of this attitude and a discovery the consequences of which have revolutionized the practice of medicine. Although the least inquisitive layman cannot have been unaware that a remarkable advance has taken place, its magnitude and significance seem sometimes not to be fully appreciated even by those more directly concerned: the effective control of formerly dangerous diseases by the mere swallowing of tablets has become a matter of course. The acute infections which respond best to this treatment are those which were often fatal in youth or the prime of life—pneumonia, cerebro-spinal fever, child-bed fever and septic infection of all kinds, whether involving war wounds or other gross injuries, or originating in some more trivial way but leading to a state so often formerly described in inquest reports as 'blood-poisoning.' These last were cases before which medical science stood almost powerless: they are now as amenable to treatment as they were formerly resistant. The origin of these and other developments of bacterial chemotherapy was the synthesis by MIETZSCH and KLARER of the drug known as prontosil, and the disclosure of its therapeutic properties by DOMAGK. Whereas this original discovery was made in German laboratories, the immense developments which have proceeded from it are due in the first place to an observation made in France, and subsequently in the main to work in Great Britain and the United States.

Prontosil was one of a long series of azo compounds which had been tested for therapeutic activity in mice. Its discovery was thus purely empirical, and the nature of its action was unknown. It was first postulated by French workers, the TRÉFOUELS, NITTI and BOVET, and confirmed by FULLER in England, that prontosil



is broken down in the body, liberating its active constituent, *p*-aminobenzene sulphonamide,

a compound now known almost universally as sulphanilamide, although also unfortunately by a large number of confusing trade names. In spite of German opposition to this belief, it was soon established that prontosil owed its therapeutic activity to this constituent, and sulphanilamide itself, which had advantages in greater solubility and more rapid absorption, came into therapeutic use in place of prontosil.

This further discovery has led to the synthesis of innumerable further compounds based on the sulphanilamide molecule, in the hope of obtaining improved effect or of extending the effective scope of this treatment to other diseases. It is beyond dispute that the greatest single advance on these lines was the introduction in 1938 of 2-*p*-aminobenzenesulphonamido-pyridine for the treatment of pneumonia. This drug, known as sulphapyridine, or 'M. and B. 693,' was synthesized by A. J. EWINS and tested experimentally by L. E. H. WHITBY of the Middlesex Hospital. It filled the most serious gap in the capacity of these drugs to arrest acute and frequently fatal bacterial infections. Most of the varied manifestations of infection by streptococci had been controlled by sulphanilamide, but this drug had little action on the closely related pneumococcus, the principal cause of pneumonia, a disease which the late SIR WILLIAM OSLER, borrowing a phrase from John Bunyan, described as 'Captain of the Men of Death.' The effect of sulphapyridine in most cases of pneumonia is dramatic; the mortality of the disease has fallen from a general average of about 25 per cent. to the region of 5 per cent., and the number of lives saved, although entirely beyond computation, probably exceeds the total to the credit of chemotherapy in all other bacterial infections put together. The evaluation of this treatment in adequately controlled studies on a large scale has been carried out mainly in the United States, whence also has recently come another drug, 2-sulphanilamido-pyrimidine ('sulphadiazine'), now in increasing demand not merely for its efficacy, but because it can be taken in large doses without causing the nausea and depression produced by others. This and other advantages are claimed for sulphamethazine [2-(4'-aminobenzenesulphonylamino) 4 : 6-dimethyl-pyrimidine], a new British product the action of which is now being studied before it is made generally available.

Of wider interest than the conquest of any particular infection has been the problem of how these compounds act. They do not behave like ordinary antiseptics, killing bacteria in the test-tube within a few minutes. Prontosil has in fact no action whatever on bacteria outside the body, and that of sulphanilamide is unimpressive when tested by ordinary methods, consisting only of a capacity for preventing the growth of small numbers of bacteria rather than the ability to destroy many outright. It was therefore natural that some mode of action in the body should have been suspected other than one directly lethal to bacteria: the complexity of the processes both of microbic attack and of bodily defence is such that there are many points at which interference might occur. Apart from several hypotheses of this kind, there have been two extreme schools of belief, one of which has been voiced chiefly in Germany by Domagk [1] himself and others. Their attitude has been one of almost reverent agnosticism, as if the progrees of events in an area of infection in the living body subject to chemotherapy held secrets which our present knowledge cannot hope to master. To call a remedy 'echt Chemotherapeuticum' is for them to elevate it to a plane of impenetrable mystery. The extreme opposite of this belief, which has perhaps been more widely held, I expressed myself [2] as long ago as May 1938 and have maintained since; it is that sulphonamide compounds have no occult or indirect action, but check bacterial growth in the body by some interference with the processes necessary for their multiplication. This in itself is enough to secure their destruction, both because bacteria kept at the temperature of the body must either grow or die, and because acute infections progress only by very rapid bacterial multiplication; if this should cease, the growing strength of the forces of defence will inevitably prevail.

It is now known that this is the true explanation, and we can moreover understand precisely how sulphonamide compounds interfere with bacterial growth. For the history of how this discovery came about, we must go back ten years to the foundation by P. FILDES of a laboratory at the Middlesex Hospital for the study of bacterial metabolism. From the time of PASTEUR to the present day bacteria have been cultivated in media containing meat extracts; Pasteur used 'bouillon nutritif,' and 'broth' is still the name of a medium universally employed. For everyday purposes it is enough that most bacteria will grow in a medium composed of meat extract and peptone, the only object being that they

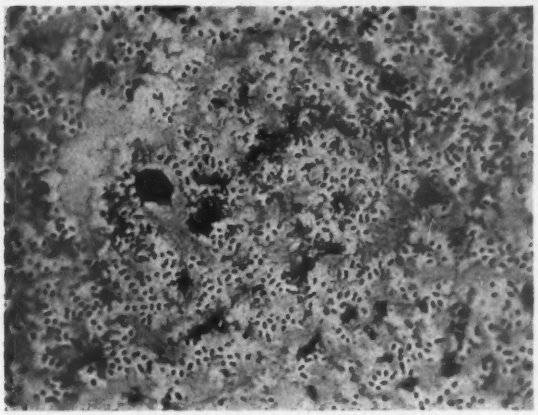


FIGURE 1 (*a*) – *Pneumococci showing normal morphology (elongated deeply stained cocci, chiefly in pairs, and of uniform size).*

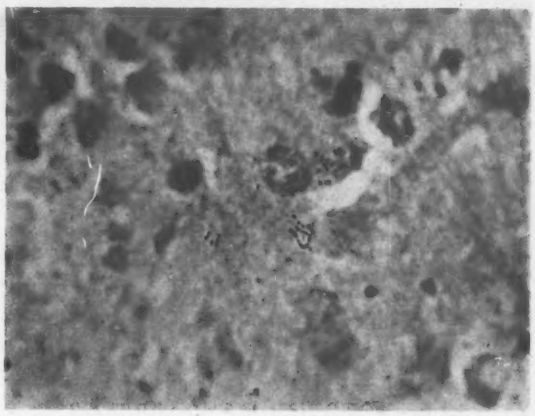


FIGURE 1 (*b*) – *Pneumococci in pus from an abscess unrecognized and untreated for several months. If such a condition remains localized, many of the bacteria degenerate and die, and swollen, shrunken, and poorly staining forms are produced.* (× 475)

should grow. But it would clearly be of great advantage to the fundamental understanding of bacterial activity to know in exact chemical terms what nutritive elements are necessary for their growth. These can only be identified by using media consisting of pure, and preferably synthetic, ingredients, starting in any given case with the simplest possible constitution and making additions until growth is secured. By this method Fildes and his collaborators have amassed extensive and valuable data, and identified various previously unknown 'factors' necessary for the growth of different bacterial species. Having in the course of this work exactly ascertained the growth requirements of streptococci, they were in a unique position to study any effect on the growth of this micro-organism produced by sulphanilamide.

The actual approach to this problem was made in a peculiar way, and owes something to the work of others. J. S. LOCKWOOD [3] of Philadelphia first observed that the restraint of bacterial growth by sulphanilamide *in vitro* is prevented by peptone: this is a constituent of all ordinary culture media, and its presence thus accounts for the unimpressive results of earlier tests. It had long been known that growth-restraint fails when the initial number of bacteria is large, and T. C. STAMP [4] and H. N. GREEN [5] followed this up by showing that a substance can be extracted from streptococci themselves, and from other bacteria, which antagonizes the action of sulphanilamide. Fildes' colleague D. D. WOODS [6] then found that this substance existed in yeast, and since this was a prolific source he was able to fractionate it and test each fraction for its capacity to antagonize the action of sulphanilamide on streptococci in a synthetic medium. By this laborious process he succeeded in identifying the substance concerned as *p*-aminobenzoic acid. Whether obtained from yeast or independently synthesized, it quantitatively neutralizes the action of sulphanilamide on bacteria *in vitro;* it also completely prevents curative action in the infected animal body. These astonishing facts are simply explained. It is now known that *p*-aminobenzoic acid is essential for the nutrition of streptococci and some other bacteria. They can form it themselves, but its further utilization depends on an enzyme reaction which is inhibited by sulphanilamide. An essential stage in the building up of some necessary constituent of the bacterial cell is thus interrupted. In the nutritive environment furnished by the infected mammalian body, the concentration of sulphanilamide which can be produced by ordinary dosage in the blood, and therefore throughout the tissues, achieves this effect. That the death of bacteria under the influence of these drugs is simply death from inanition might well be deduced from the accompanying figures, one illustrating bacteria dying slowly and naturally in a closed abscess cavity probably months old, the other showing the effect on them produced by sulphapyridine in only two days. The degenerative changes are of the same nature in each case.

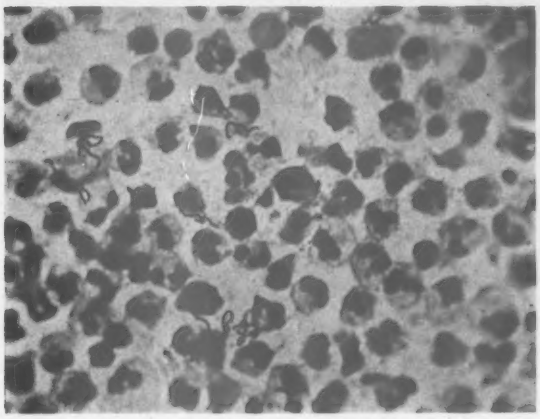


FIGURE 2 (*a*) – Streptococcus pyogenes *in pus, showing normal morphology (long curved chains of cocci of uniform size and staining uniformly; the large spherical cells in the background are leucocytes).*

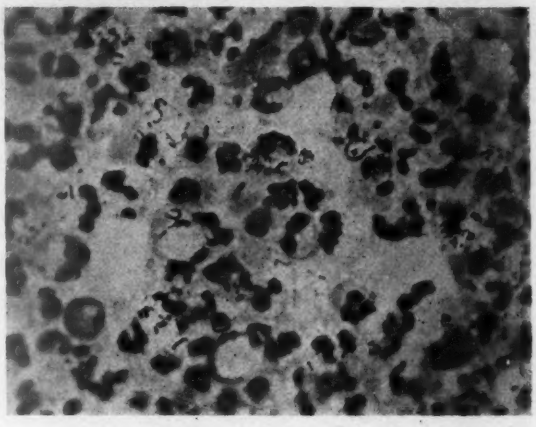


FIGURE 2 (*b*) – *The same micro-organism from an abscess only three days old in a patient treated with sulphapyridine. There is gross irregularity in size and shape, and many of the cocci stain poorly (cf. figure* 1 (*b*)). (× 475)

The profound significance of this discovery needs no emphasis. By laying bare the exact mechanism underlying the greatest therapeutic discovery of modern times it has opened the way to its extension on rational instead of merely empirical lines. It has had a more immediate and practical effect in encouraging and justifying the local application of these drugs in powder form to wounds, a measure which has proved of immense value, particularly in war surgery.

No review of progress in this sphere would be complete without reference to the astonishing observations recently made on the extraction of antiseptic substances from micro-organisms themselves. Whether by chance or as part of the antagonism between species which occurs so often throughout both animal and vegetable kingdoms, certain micro-organisms do produce substances highly inimical to others. Penicillin, a hitherto unidentified substance formed by the mould *Penicillium notatum*, is a powerful antiseptic, and nothing stands in the way of what bids fair to be a valuable use for it in medicine except difficulty of production on an adequate scale. The action of this substance was first observed by A. FLEMING at St Mary's Hospital, London, and has recently been studied by H. W. FLOREY [7] and others at Oxford. Gramicidin is the name given to a substance extracted by DUBOS [8] of New York from an otherwise quite indifferent bacillus isolated from soil; it has properties similar to those of penicillin, and has been reported [9] within the past few months to satisfy a special need in the treatment of wound infection. Here again there are prospects that chemical analysis of the underlying process may place a new form of treatment on a more assured footing. In this field of medical research, in Britain at least, war has been the incentive to rapid progress, and more has been achieved towards the control of infection, particularly of wounds, than might have followed many years of more leisurely study with less motive and material.

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Book reviews

PRACTICAL EXERCISES IN CHEMICAL ENGINEERING

The Applications of Chemical Engineering, *edited by Harry McCormack. Pp. x + 431. Chapman and Hall Limited, London.* 1940. 21*s.*

The title of this book is rather unfortunately chosen and hardly serves to indicate its scope. It is actually a practical laboratory manual in chemical engineering intended to furnish suitable practical exercises for a university course. The work is a co-operative effort of a dozen authors, all engaged in the teaching of chemical engineering at various American universities. It owes its origin largely to the work of two committees of the Society for the Promotion of Engineering Education, which collected together a considerable amount of material on appropriate laboratory instruction.

The book consists of eleven chapters dealing with the most important unit operations of chemical engineering. Although the chapters are by different authors, the general method of treating each operation is the same. After a short exposition of the general theory underlying the unit operation, a number of practical exercises are set out in detail. In connection with each exercise, there are given a statement of its object, a description of the equipment, an outline of the procedure to be followed, and the method to be adopted in reporting the results of the exercise. In all, there are seventy-two exercises included in the book, and a fairly wide choice is thus available to meet local conditions in any particular laboratory. The exercises have all been carefully chosen, satisfactorily tested over a number of years, and designed for use with reasonably simple equipment that should be readily available or easily constructed. Each exercise is designed to bring out basic theoretical principles and to be capable of being carried through in a four-hour laboratory period.

The book is a most valuable contribution to the literature on chemical engineering education and covers a subject which has otherwise been dealt with very sparsely in the published literature. It will certainly be appreciated in this country, where chemical engineering education has not yet developed on the same scale as in the United States, and it can be used without any material adaptation for educational conditions here. In the teaching of any branch of engineering, practical laboratory work is an essential part, as it constitutes the bridge between the abstract scientific principles and their practical applications which the student will later meet with in industry. Careful planning of these practical exercises is most important if the limited time of the student's course is to be utilized to the best advantage. At the same time, it is vitally necessary to avoid exercises of the 'cookery-book' type.

The contributions of the various authors of the book have been well co-ordinated as far as subject-matter is concerned, but less successfully in some points of detail. A marked example is the different methods adopted in various chapters for dealing with references to the literature. There are more printing errors than one expects in a work of this standard, and many minor omissions in the references. No doubt these slight blemishes will be removed in a later edition.

A. J. V. UNDERWOOD

INDUSTRIAL PLASTICS

Plastics in Industry, *by 'Plastes.' Pp. xiii + 248. Chapman and Hall Limited, London. Second edition,* 1942. 15*s. net.*

The main aim of this book is to give those engaged in industry a working knowledge of plastics which will enable them to apply these modern materials of construction to their own everyday problems. That a second edition of the original work was called for nine months after the first is sufficient testimony both to the efficiency with which this aim has been attained and also to the growing interest which technologists are taking in plastics. The first four chapters are devoted to a review of the fundamentals of the industry, beginning with definitions of technical terms involved, a description of the most important thermosetting and thermoplastic materials used, the methods of moulding and fabricating them, and the standard specifications now accepted to control them. Thus the potential user is provided with adequate data which will give him at any rate the preliminary indications as to whether he may expect specific plastics to serve his purpose.

The remainder of the book is devoted to a survey of the part plastics were playing in industrial and domestic life prior to the outbreak of the present war. As far as possible, data have been modernized in the second edition, but for obvious reasons the full part plastics are playing in the war effort must be reserved for a post-war edition. A chapter has been added dealing with the recent applications of plastics to thermal insulation, a field in which these new materials have already shown themselves far superior to the conventional products.

Many of the small inaccuracies which crept into the original publication have been corrected in the new edition. There are also considerably more illustrations. A brief review is provided of available technical literature. The book is well produced and should be in the hands of all those who handle constructional materials; they will find it a useful guide to the shape of things to come.

V. E. YARSLEY

THE STORY OF RUBBER

Rubber and its Use, *by Harry L. Fisher. Pp.* xvi + 128, *with a frontispiece and* 20 *figures. Macmillan & Company Limited, London.* 1942. 7*s.* 6*d. net.*

Rubber manufacturers in the past have been very much like the doctors—reluctant to discuss their art with their contacts. Both were inspired with the same idea, namely that the customers and patients respectively would be better off by knowing nothing about the subject. The result of this attitude in the former case is that to the layman, with one exception, 'rubber' is 'rubber,' whether it is raw or vulcanized: the one exception is 'red rubber,' which is mysteriously supposed to have good ageing characteristics quite independent of how it has been compounded. This attitude is now changing, largely owing to the fact that the rubber manufacturers' customers are now no longer only the man in the street, but technical organizations which have a habit of asking what they are buying.

In this and other ways a general interest in rubber has developed. Recent events in the Far East have greatly strengthened this popular interest and extended it even to synthetic rubber. The author of this little book states that it is the outcome of the interest shown by the audiences when he

lectured to such varied groups as chemical societies, college student groups, high school assemblies, men's clubs, women's clubs, and luncheon clubs. What more proof is needed of the general interest in rubber at the present time? Furthermore, the author has based his book upon the questions asked by these audiences, but it should not be concluded that this has in any way narrowed the scope of the book, since every aspect and field of rubber technology have been touched upon in an interesting way.

It is a book which everyone connected with the management of rubber technical organizations has been looking for, to put into the hands of their newcomers. To the general reader it will be a mine of information. The rubber technologist, in spite of the fact that most of the contents will be well known to him, will read the book with pleasure since he will sense the enthusiasm of Dr Fisher for this fascinating subject. W.J.S.N.

DEPLETION OF THE SEA

The Overfishing Problem, *by E. S. Russell. Pp. viii* + 130. *Cambridge University Press, London.* 1942. 7*s.* 6*d. net.*

Some eighty years ago the Royal Commission on Fisheries recommended that all restrictions on fishing should be repealed. The population of food fishes was then adequate to withstand the attentions of sailing vessels fishing with lines and the relatively small beam trawl. But towards the end of the last century steam began to replace sail and the powerful steam trawlers employed the larger, more efficient otter trawl. Ever greater harvests were drawn from the sea bottom. Although the effects of this were for some time offset by the development of new fishing grounds from the Barents Sea to the coasts of Morocco, yet gradually statistics of landings disclosed the dire effects of overfishing in decreased catch per day of fishing and in decline in the size of the fish.

The demonstration of the fact of overfishing, together with the discussion of preventive measures, form the joint themes of DR RUSSELL'S book. As Director of Fishery Investigations to the Ministry of Agriculture and Fisheries he writes with unique authority on this subject. His figures reveal that, despite increasing intensity of fishing, the yield in most areas remains either stationary or shows an actual decline. The reduction of fishing during the last war caused only a temporary improvement.

Dr Russell shows that two things are wrong. First, there has been too much fishing, so that the catch has fallen below the possible steady maximum which the reproductive powers and rate of growth of the fish can support; and, second, too many undersized fish are destroyed. The latter evil can be cured by an increase in the mesh of the nets, the beneficial effects of which have been experimentally proved. Only an agreed international reduction in the volume of fishing can cure the first. Such an agreement, between the United States and Canada, saved the halibut fishery of the North Pacific when this was similarly threatened.

Our fisheries are likely to be of the greatest importance after this war, when we may be thrown back more on our own resources. Dr Russell is to be congratulated on the production of a book which lays down the basis of a planned economy of post-war fishing. C. M. YONGE

SCIENCE IN THE GARDEN

The Living Garden, *by E. J. Salisbury. Pp. xi* + 232. *G. Bell & Sons Limited, London. Second edition,* 1942. 6*s. net.*

This book is already well known to a wide circle of readers, and we welcome its appearance in a revised and cheaper edition. Few authors know more of plant-life than PROFESSOR SALISBURY, and still fewer combine this knowledge with an aesthetic appreciation of gardens and an ability to express both knowledge and appreciation in plain English. All garden-lovers who wish to understand the main principles of the plant-life they nurture will here find an interesting and reliable guide. The illustrations are numerous and well chosen, and the book as a whole is delightful: scientists will take particular pleasure in the thought that T. E. BROWN would probably have disliked it intensely.

AN INTRODUCTION TO ASTRONOMY

Foundations of Astronomy, *by W. M. Smart. Pp. vii* + 268, *with* 119 *figures. Longmans, Green & Company Limited, London.* 1942. 16*s. net.*

Astronomy is a subject that has been almost entirely omitted from general science courses in Great Britain. This neglect is as surprising as it is deplorable, for astronomy touches everyday life at many points. To it is due the widespread ignorance of the simplest celestial phenomena and their consequences—such as the northward and southward movements of the Sun in the course of the year, the retardation in the times of rising and setting of the Moon from night to night, the difference between sundial time and mean time, the differences in blackout times for various towns, the phases of the Moon, the changing appearance of the sky in the course of a night and from one season to another, and so forth. To it may probably also be traced the widespread and increasing faith in the predictions of astrologers. The SPENS report made the recommendation that some astronomy should be included in all general science courses; there is hope for the future if this recommendation is implemented.

The war has not only made clear the widespread need for a background of astronomical knowledge, but has also provided better opportunities for the study of celestial phenomena. The Observer Corps, Home Guards, fire watchers and others have had excellent opportunities for observing the sky and the movements of stars, planets and the Moon. There has been an increasing demand for planispheres and popular books on astronomy. The use of the stars for providing direction at night is becoming more and more recognized, though it does not yet form part of the training of every soldier, sailor, and airman, as it should do. The Sun, Moon, stars and planets provide the best and least fallible method of air navigation.

This book, by the Regius Professor of Astronomy in the University of Glasgow, is intended primarily for students taking a first-year course in astronomy in the universities. The treatment is essentially mathematical, but no mathematical knowledge beyond elementary trigonometry and the use of logarithms is assumed. It covers, as the title suggests, and in brief compass, the basic foundations on which the whole science of astronomy has been built. One chapter is devoted to the problem of navigation and determination of position on the Earth. Numerous examples, to illustrate points of theoretical and practical interest, are provided. Anyone who has mastered this book will have acquired a solid foundation of astronomical knowledge, which can be extended according as his needs require or his inclinations suggest. H. SPENCER JONES

Notes on contributors

SIR ROBERT ROBINSON,
M.A., D.Sc., Hon.D.Sc., Hon. LL.D., F.R.S.

Was born in 1886, the son of the first inventor-manufacturer to make pill-boxes, surgical lint, and cotton bandages by machinery. He was educated at Fulneck School, near Leeds, and the University of Manchester. Appointed Professor of Organic Chemistry at the University of Sydney in 1912, he has since held several professorial chairs, and is at present Waynflete Professor of Chemistry in the University of Oxford. His scientific work has been concerned with the structure and synthesis of such natural products as alkaloids and anthocyanins, and with the application of electronic theories to the mechanism of reactions. He has been president of the Chemical Society of London and is a medallist of the Royal Society and many other learned bodies. A keen mountaineer, he says that his 'chief vice, a bad one, is chess.'

C. D. DARLINGTON,
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Born in 1903, he went to St Paul's School, London, but left at the age of 16 'and never regretted it.' He became a pupil of William Bateson at the John Innes Horticultural Institution in 1923, and was appointed Director of the Institution in 1939. He is well known for his original investigations on heredity, and in his *The Evolution of Genetic Systems* (1939) he used chromosome studies to establish a new point of view in biology. He prefers Lucretius, Stendhal and Lytton Strachey to most other writers, likes Mozart better than Sullivan, and detests lawyers, letter-writing and empire-builders.

J. KENDALL,
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Is Professor of Chemistry in the University of Edinburgh, though a native of the 'degenerate South,' having been born at Chobham, Surrey, in 1889. He was educated at Farnham Grammar School, the University of Edinburgh, and the Nobel Institute, Stockholm. From 1913–26 he held a professorial chair of chemistry in Columbia University, New York City, and later was Professor of Chemistry in Washington Square College, New York University. During the first world war he served as Lieutenant (later Lieutenant-Commander) in the U.S. Naval Reserve. After two years as Dean of the Graduate School, New York University, he was translated in 1928 to his present post at Edinburgh. He has made numerous contributions to the progress of chemistry, and has been particularly successful in interpreting chemistry to the layman.

SIR EDWARD APPLETON,
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Is a native of Bradford, Yorkshire, where he was born fifty years ago. After occupying professorial chairs of physics at both London and Cambridge he became, in 1939, Secretary of the Department of Scientific and Industrial Research. As a member of the Scientific Advisory Committee of the War Cabinet, he is much behind the scenes in the scientific war effort. His own researches have been principally directed towards the exploration of the upper air by means of radio waves, in the course of which he led a British radio expedition (1932–33) to Tromsö, in Northern Norway, to study the effect of the aurora on radio transmission. In 1926 he discovered the ionized atmospheric layer which now bears his name, and which makes round-the-world radio communication possible. He has been active in promoting co-operation in the field of radio science, and is President of the International Scientific Radio Union. He was Hughes Medallist of the Royal Society in 1933, and was awarded the Morris Liebmann Memorial Prize of the American Institute of Radio Engineers. He has had research pupils from all over the world to learn ionospheric technique developed in this country.

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Born at Wells, Somerset, in 1882, he was educated at Sexey's School, Bruton, and Emmanuel College, Cambridge, of which he is now a Fellow. In 1936 he was elected Professor of Botany in the University of Cambridge after long service as Lecturer and Reader. In 1914 he was Government Mycologist in the Federated Malay States, and during the last war was Plant Pathologist in the Food Production Department. His book *Plant Diseases* is well known, and he has trained a large number of plant pathologists now serving in different parts of the Empire. He is one of the General Secretaries of the British Association and a member of the Agricultural Research Council. A keen gardener, he claims that his gardening experience has been of great assistance to him as a botanist and plant pathologist.

E. G. RICHARDSON,
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Was born at Watford in 1896 and was educated at Coopers' Company's School and University College, London. In peace-time he is the Senior Lecturer in Physics at King's College, Newcastle-upon-Tyne (University of Durham). He served in the R.A.F. in the war of 1914–18, and in this one is engaged on research in acoustics and hydrodynamics for the Services. He has specialized in the physics of sound—a subject to which he was drawn by his interest in music—and has written many books and papers on acoustics as well as on the general applications of physics.

L. P. GARROD,
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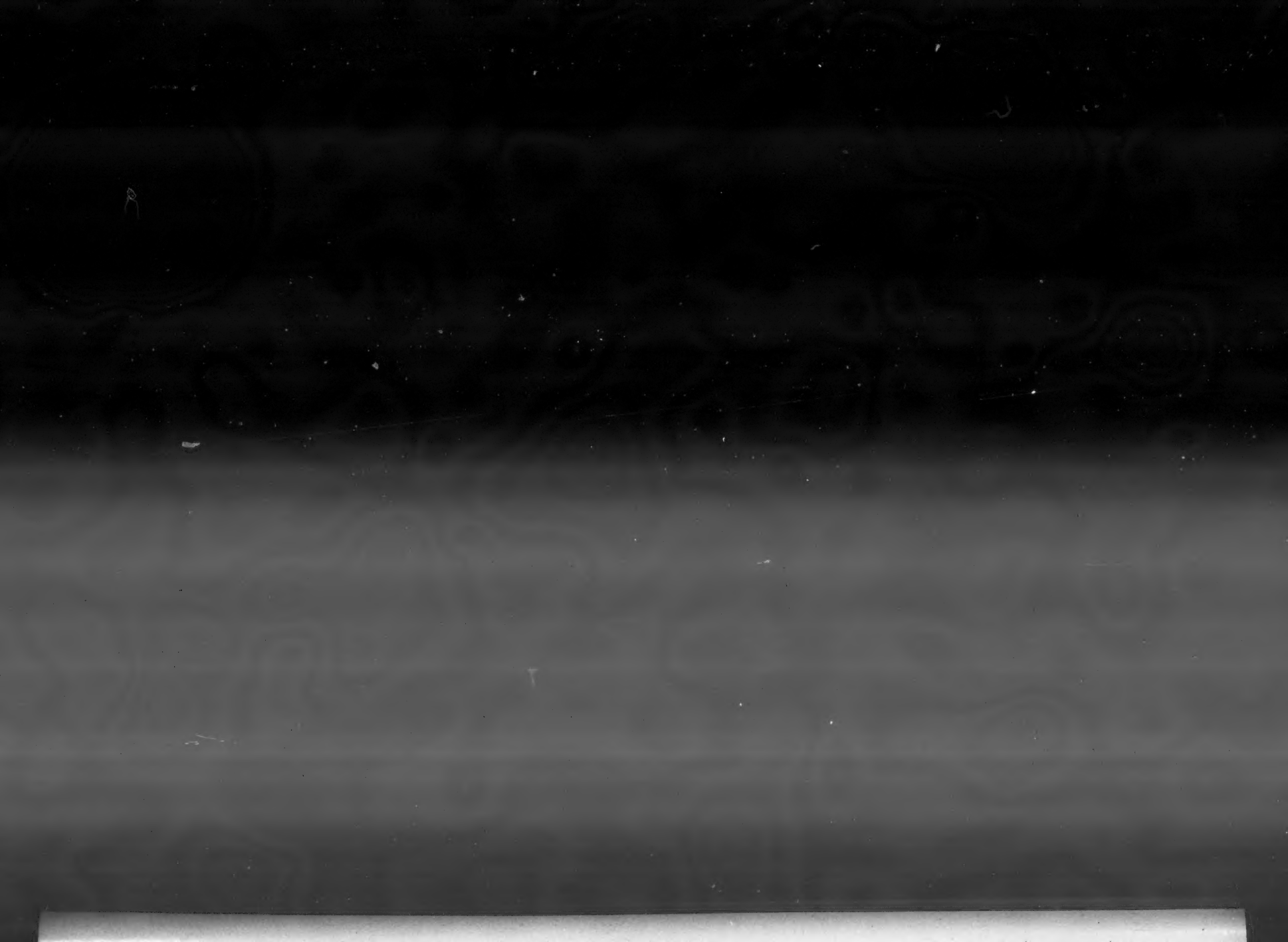
Is Bacteriologist to St. Bartholomew's Hospital and Professor of Bacteriology in the University of London. He has studied the destruction of bacteria by chemical means from many different aspects, devised new methods of testing and employing antiseptics, and consistently upheld the doctrine that the defence of the body by chemical agencies against bacterial attack is feasible. Writes on the subject of bacterial chemotherapy from a close study of its development abroad as well as at home, and from clinical experience in a large hospital.

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